

American Heart Journal

VOL. 33

JUNE, 1947

No. 6

Original Communications

SIGNIFICANCE OF ABNORMALLY SMALL QRS DEFLECTIONS IN ONE OR MORE PRECORDIAL LEADS

ALBERT W. LAPIN, M.D.*

MONTREAL, QUEBEC

LOW voltage of the QRS deflections in the standard limb leads has engaged the attention of many investigators since the early days of electrocardiography, and the significance attributed to it has undergone many fluctuations. In recent years, since the use of precordial leads has become more widespread, various reports have appeared on low voltage occurring in these leads. Several attempts have been made to show some correlation linking low voltage in the two types of leads, but there has been little agreement among different writers as to whether any correlation of this kind exists. There is, furthermore, no consensus as to whether low voltage in the precordial leads is of any important significance. The present study was undertaken partly to ascertain whether low voltage in the precordial leads has, as a rule, the same or a different origin than low voltage in the limb leads and whether it should be regarded as more, or less, important.

Before proceeding to a consideration of our findings it may be profitable to review some of the earlier work on the significance of low voltage occurring in the limb leads, in the precordial leads, or in both.

EARLIER OBSERVATION ON LOW VOLTAGE

Low Voltage in the Standard Limb Leads.—Low voltage is commonly considered to be present in the standard limb leads if the greatest deflection of the

From the Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Mich.

Much of the work upon which this article is based was done with the aid of grants to Dr. Frank N. Wilson from the Horace H. Rackham School of Graduate Studies and the S. S. Kresge Foundation.

*Clinical Fellow in Medicine of the American College of Physicians for the year 1946. Demonstrator in Medicine, McGill University.

Received for publication Aug. 29, 1946.

QRS complex extends less than 5 mm. above or below the base line in all of them, when the electrocardiograph is so standardized that the introduction of 1 mv. into the circuit produces a deflection of 10 millimeters.

In 1926 three papers dealing with low voltage appeared in the American literature, and all three took a gloomy view of its significance. Sprague and White,¹ reviewing fifty-seven cases, concluded: "Excluding the temporary effect of hypothyroidism, low voltage has never been found in our experience in records from normal hearts." Hepburn and Jamieson² summed up their experience thus: "Low voltage (even when) unaccompanied by other electrocardiographic abnormalities is a prognostic sign of serious import." On statistical grounds they considered it to rank second only to bundle branch block as an electrocardiographic sign of ill omen. Master and Pardee³ included low voltage among a number of specified graphic abnormalities that are "indicative of a diseased heart."

In the following year there appeared a paper by Willius and Killins,⁴ whose conclusions were almost directly opposite to those of the previous investigators. They reported a series of 140 electrocardiograms showing low voltage as the sole deviation from the normal, and they concluded that low voltage not accompanied by other graphic abnormalities does not necessarily imply that serious myocardial damage is present. Later studies, likewise carried out on hospital patients, gave intermediate results. Turner,⁵ in 1932, reported low voltage in the standard limb leads in about 3 per cent of the routine electrocardiograms taken at the Presbyterian Hospital in New York. He analysed 164 cases and found that 113 of the patients had manifest heart disease and sixty-three of these were in congestive failure; of the remaining fifty-one patients with no organic cardiac disease, twelve had edema or fluid collections in the serous sacs. Barrit,⁶ in a hospital series of ninety-four patients, found that when low voltage was accompanied by abnormal T waves there was a much higher incidence of heart disease than when it was the sole graphic abnormality but that even in the latter case heart disease was present in 45 per cent of the patients.

One obvious reason for such divergent conclusions is that the different observers were studying records taken on selected cases and not on "random samples." Before the significance of low voltage could be critically appraised, it was necessary to know its incidence as a physiologic variant in the records of normal persons, and up to the time of the early studies mentioned, no large series of such records had been published. During the past ten years, however, a considerable number of electrocardiograms of healthy persons have been collected and studied by various authors: Table I gives in summary the incidence of low voltage in the standard limb leads in seven such series, totalling 5,500 normal persons. One study was made on a group of college students,¹⁴ two on groups of military aviators,^{9,11} others on business and professional men whose ages ranged from 30 to 60 years,^{8,12} and one series included women,¹³ so that both sexes and a wide range of ages were represented.

Of the total of 5,500 persons, only sixty, or 1.09 per cent, showed low voltage in the standard limb leads. The incidence in each of the separate series is in quite good agreement with this figure, ranging from 0 to 1.6 per cent.

TABLE I. INCIDENCE OF LOW VOLTAGE IN STANDARD LIMB LEADS OF 5,500 HEALTHY INDIVIDUALS

SERIES	TOTAL NUMBER	NUMBER WITH LOW VOLTAGE	PER CENT
Crawford ⁷	1,000	14	1.4
Johnson ⁸	2,400	26	1.09
Graybiel and co-workers ⁹	1,000	16	1.6
Stewart and Manning ¹¹	500	1	0.2
Larsen and Skulason ¹²	100	0	0
Shipley and Halloran ¹³	200	3	1.5
Bellet and Kershbaum ¹⁴	300	0	0
Total	5,500	60	1.09

It is apparent from these data that while low voltage in the limb leads may occur in the electrocardiograms of healthy persons, it is an uncommon finding, occurring not much oftener than once in one hundred observations.

One other series is mentioned separately, because its figures are quite different from the rest. This is the report of a study made on 173 civil airline pilots¹⁰ in whose standard limb leads low voltage was found in fourteen, or 8 per cent of the subjects. These pilots were in the same age group as many of the persons in the other series reported in the foregoing discussion, and it is difficult to account for the much higher incidence of low voltage. If these figures are added to the totals in Table I, then of a total of 5,673 healthy persons, there are seventy-four with low voltage, an incidence of 1.3 per cent.

Low Voltage in the Precordial Leads.—With regard to low voltage in the precordial leads, the literature contains a number of reports,¹²⁻¹⁶ but for various reasons it is not easy to compare one with another. The method of selecting cases varied from one series to another, and the several investigators did not use the same locations for either exploring or indifferent electrodes. It will probably suffice for our purpose to consider in detail only two of the papers that were published up to 1941.^{14,16} Both of these deal specifically with the pathologic significance of low voltage in the precordial leads and both contain comprehensive reviews of earlier work on the subject.

Leach, Reed, and White¹⁶ studied the relationship between the amplitudes of the deflections in the standard limb leads and their size in a single unspecified precordial lead from the region of the apex impulse (probably CF₄). They considered low voltage to be present in this lead when the voltage of the largest QRS deflections in either direction did not exceed 0.5 millivolts. They collected 100 cases with low voltage in the standard leads and normal voltage in Lead IV (Group 1); 100 cases with low voltage in Lead IV and normal voltage in the standard leads (Group 2) and 100 cases with low voltage in both (Group 3). They found evidence of heart disease in 57 per cent of the total composite series of 300 cases: in 65 per cent of Group 1 and in 63 per cent of Group 3 but only in 47 per cent of Group 2 (low voltage in the precordial lead alone). They con-

cluded that not only heart disease, but also general debilitating diseases, changes in the position of the heart, and changes in the conductivity of the adjacent tissues are factors in the production of low voltage; and that, in addition, the thickness of the chest wall and the position of the precordial electrode (they were using only one precordial lead) influenced the voltage of QRS in Lead IV. It was their opinion that the finding of low voltage QRS deflections, whether in the limb or the precordial leads, is, by itself, of little diagnostic value. Since 10 per cent of their entire series of 300 individuals were perfectly healthy, it did not appear to furnish a valuable clue as to the presence or absence of cardiac or noncardiac disease.

Bellet and Kershbaum,¹⁴ studying the same problem, arrived at a rather different conclusion. They collected twenty cases showing low voltage in both limb and precordial leads. In each of these, three precordial leads had been taken, and they required that all show small deflections before low voltage was considered to be present. Most of these cases had been studied before the American Heart Association and the Cardiac Society of Great Britain and Ireland had announced the joint recommendations of their Committees on Standardization of Precordial Leads,¹⁷ and the chest leads used were not, for the most part, those later recommended. They consisted of one from apex to left leg, one from apex to back, and one from left scapula to left leg, so that only one of the precordial positions specified by the Committees on Standardization was included, namely, the region of the apex impulse. In all twenty patients there was evidence of severe myocardial damage, and in eleven myocardial infarction was present. In a control group of fifty patients with low voltage in the limb leads, but normal voltage in the precordial leads, the incidence of severe myocardial damage was much less. It was concluded that whereas the limb leads might show low voltage as a result of extracardiac factors such as edema, serous effusion, emphysema, or an unusual position of the heart in the thorax, the precordial leads are not, as a rule, affected by such factors, and low voltage in these leads is due in almost all cases to serious myocardial disease.

MATERIAL AND METHODS EMPLOYED IN THE PRESENT STUDY

Our material consisted of 100 electrocardiograms showing low voltage in the standard limb leads, drawn in chronological order from the files of the Heart Station and each accompanied by a full set of six precordial leads. These 100 cases were then separated into two main groups, depending on whether or not low voltage occurred in any of the precordial leads as well. The precordial leads were taken from the chest positions C_1 to C_6 specified by the Committees on Standardization,¹⁷ with Wilson's central terminal¹⁹ as the indifferent electrode.

In a series of this type, collected in a hospital, an element of special selection is inevitably introduced, because it is the practice in most clinics to order electrocardiograms only on patients who are strongly suspected of having heart disease; moreover, patients with certain types of cardiac disease are more likely to have precordial leads ordered than are others. The resulting series can therefore hardly be considered a random sample of the general population, or even

of the hospital population. This defect in sampling is freely acknowledged, but it need not be given too much weight in the case of the present study, since we do not intend to draw any broad conclusions as to the numerical incidence of specific diseases associated with low voltage but rather to ascertain what physiologic changes are common to the various types of case in which low voltage occurs.

Criteria for Low Voltage.—In the standard limb leads the specifications of the Criteria Committee of the New York Heart Association³¹ were adopted, low voltage being considered to be present when the greatest deflection of the QRS complex does not extend more than 5 mm. above or below the base line in any of the three leads.

It was more difficult to arrive at a satisfactory definition of low voltage in the precordial leads. Others have applied to these leads the same criteria as in the case of the standard limb leads, but it seemed to us that this was hardly justifiable since the mean size of the deflections in the precordial leads is normally so much greater. It was necessary as a preliminary step to consider the range in amplitude of the ventricular deflections in the precordial electrocardiograms of healthy individuals whose curves had been taken with the same technique as that used in our cases. In this way a standard minimal voltage could be set for each lead, and any considerably smaller voltage could reasonably be designated as low. Two studies satisfactory for our purpose have been reported.

Kossmann and Johnston,¹⁸ using Wilson's central terminal and the chest positions C₁ to C₅, studied the precordial Leads V₁, V₂, V₃, V₄, and V₅ in thirty normal students. Table II represents a condensation of some of their findings: it lists the minimum, maximum, and mean values for the amplitude of the R, S, and RS deflections in each lead. The RS, or intrinsic deflection in any lead, is measured by adding the voltages of the R and S deflections; this gives a truer representation of the magnitude of the potential variations than does the largest QRS deflection measured from the base line. The minimum values found for the RS deflection were 1.5 mv in Lead V₂, 1.26 mv in Lead V₃, 1.8 mv in Lead V₄, and 1.12 mv in Lead V₅.

TABLE II. MEASUREMENTS OF THE QRS DEFLECTIONS IN THE PRECORDIAL LEADS, EXPRESSED IN TENTHS OF A MILLIVOLT*

LEAD	R			S			RS		
	MIN.	MAX.	MEAN	MIN.	MAX.	MEAN	MIN.	MAX.	MEAN
V ₁	1.0	9.6	4.16	3.4	24.0	11.05	6.6	26.8	15.21
V ₂	4.0	20.8	9.05	3.0	38.8	16.23	15.0	46.0	25.27
V ₃	6.0	54.6	16.70	0.0	22.0	9.05	12.6	54.6	25.75
V ₄	12.2	46.0	22.31	0.0	16.0	5.32	18.0	51.6	27.63
V ₅	8.8	33.0	18.78	0.0	9.6	1.93	11.2	33.2	20.70

*Adapted from Kossmann and Johnston.¹⁸

Bryant,²⁰ using the same technique, measured the RS deflection in Leads V₂ and V₄ in the electrocardiograms of 103 normal persons. In each of these leads the minimum voltage was 1.0 millivolts.

If the findings in these two series are combined, then the minimum values for the RS deflection in each lead are: 1.0 mv in Lead V₂, 1.26 mv in Lead V₃, 1.0 mv in Lead V₄, and 1.12 mv in Lead V₆.

Neither Kossmann and Johnston nor Bryant included Lead V₆ in their studies. This is a lead from the left midaxillary line at the level of the apex impulse. It has perhaps a closer relationship to the standard limb leads than have most of the other precordial leads, since it is influenced chiefly by electrical forces more nearly in the frontal plane. In order to ascertain the range of its amplitude in normal individuals as well as to add to the number of cases in which the other precordial leads had been studied, we measured the intrinsic deflections of Leads V₂, V₃, V₄, V₅, and V₆ in 100 cases with normal amplitude in the limb leads. These were not necessarily all normal records, but we did exclude cases of anterior, lateral, and posterolateral infarction, since these are commonly the cause of small QRS deflections in Leads V₄, V₅, and V₆. In these 100 cases, an RS deflection of 0.9 mv or less occurred only once in Lead V₂, twice in Lead V₃, once in Lead V₄, and in no case in Lead V₅, and an RS of 0.7 mv or less occurred only twice in Lead V₆. Accordingly it appeared reasonable to accept as arbitrary values for low voltage a total RS deflection of 0.9 mv or less in Leads V₂, V₃, V₄, V₅ and of 0.7 mv or less in Lead V₆. These figures are all well below the minimum values found by Kossmann and Johnston and by Bryant.

Low voltage in Lead V₁ was not considered to have any significance for our purpose, since there is quite a wide variation in the amplitude of its deflections in normal persons.

RESULTS

Using the criteria specified, we found that of the main group of 100 patients showing low voltage in the standard limb leads (to which we shall for convenience hereafter refer as Group A), sixty-five (to be designated subgroup B) showed low voltage in one or more of the precordial leads as well. Table III shows the distribution by diagnosis of the patients in both main group and subgroup. In both, the commonest diagnosis was myocardial infarction, which was present in forty-three of the 100 in the main group and thirty-five of the sixty-five in the subgroup. Of the remaining fifty-seven patients in the main group, thirty-seven had extracellular collections of fluid (hydrothorax, hydropericardium, ascites, marked congestion or edema of the lungs, or subcutaneous edema) and two had pronounced pulmonary emphysema. In the subgroup there were thirty patients without myocardial infarction and of these, nineteen had extracellular collections of fluid (twelve had hydrothorax, six had marked congestion or edema of the lungs, one had subcutaneous edema only) and one had pulmonary emphysema.

In the main group there were six patients and in the subgroup four patients with no evidence of heart disease and without extracellular fluid accumulations, obesity, emphysema, or hypothyroidism.

TABLE III. GROUP A, 100 PATIENTS IN WHOM LOW VOLTAGE OCCURRED IN STANDARD LIMB LEADS; SUBGROUP B, 65 OF PATIENTS IN GROUP A IN WHOM LOW VOLTAGE OCCURRED IN PRECORDIAL LEADS ALSO

	GROUP A			SUBGROUP B		
Myocardial infarction						
With extracellular fluid						
Hydrothorax, etc.	7			7		
Pulmonary congestion or edema	11			7		
Peripheral edema only	2			0		
Total with extracellular fluid		20			14	
Without extracellular fluid		23			21	
Total myocardial infarcts			43			35
Arteriosclerotic heart disease						
With extracellular fluid						
Hydrothorax, etc.	7			4		
Pulmonary congestion or edema	10			6		
Peripheral edema only	9			1		
Total with extracellular fluid		26			11	
Without extracellular fluid		8			4	
Total arteriosclerotic heart disease			34			15
Constrictive pericarditis, with hydrothorax			4			3
Hodgkin's disease, with hydrothorax			1			1
Carcinoma of liver, with ascites			1			0
Foreign body in heart, with hydrothorax			1			1
Metastatic carcinoma of heart, with hydrothorax			1			1
Massive pulmonary embolus with gangrenous infarct			1			0
Rheumatic heart disease, with hydrothorax			3			2
Rheumatic heart disease, peripheral edema only			1			0
Idiopathic cardiac hypertrophy			2			2
Pulmonary emphysema, severe			2			1
No heart disease (no emphysema, serous effusion, edema, obesity, or myxedema)			6			4
Total			100			65

Table IV lists in detail the sixty-five cases included in subgroup B, all showing low voltage in one or more of the precordial leads as well as in the standard limb leads. It gives the age, sex, diagnosis, height of the P and T waves, presence or absence of serous effusion, congestion of the lungs, and peripheral edema; and it gives the amplitude of the RS deflection in each of Leads V_4 , V_5 , and V_6 , as well as in the lead in which it is greatest.

It will be noted that in only three instances were the deflections low in all six precordial leads. One of these patients had a hydropneumopericardium; one had cardiac hypertrophy of undetermined etiology, without congestive failure; the third was a young woman, 31 years of age, without evidence of any organic disease.

Low voltage occurred in three precordial leads in twelve cases; in two leads in twenty-six cases; and in a single lead in twenty-four cases.

It occurred in Lead V_2 in three cases, in Lead V_3 in four cases, in Lead V_4 in twenty-two cases, in Lead V_5 in forty cases, and in Lead V_6 in fifty-six cases.

TABLE IV. MEASUREMENTS OF RS, P, AND T DEFLECTIONS IN TENTHS OF A MILLIVOLT

CASE	SEX	AGE	RS V ₄	RS V ₆	RS V ₆	LARGEST RS DEFLECTION	P	T	CLINICAL DIAGNO IS	PLEURAL OR PERICARDIAL EFFUSION OR ASCITES	CONGESTION OR EDEMA OF THE LUNGS	PERIPHERAL EDEMA	OTHER CLINICAL FEATURES
1	M	38	10	6	9	V ₂ 25	1.5	4.0	Myocardial infarction	0	0	0	
2	M	54	9	4	4	V ₂ 14	0.75	3.0	Myocardial infarction	0	0	0	
3	M	41	6	1	4	V ₂ 22	2.0	2.5	Myocardial infarction	0	0	0	
4	F	49	14	14	7	V ₂ 14	1.0	2.5	Myocardial infarction	0	0	0	
5	M	57	17	7	5	V ₂ 30	1.0	0.5	Myocardial infarction	0	0	0	
6	F	55	7	4	5	V ₂ 17	2.0	1.0	Myocardial infarction	0	0	0	
7	M	45	23	14	2	V ₂ 23	1.5	0.0	Myocardial infarction	0	0	0	
8	M	46	8	8	7	V ₂ 18	1.5	0.5	Myocardial infarction	0	0	0	
9	M	53	13	7	9	V ₂ 17	1.0	2.0	Myocardial infarction	0	0	0	
10	M	40	20	18	7	V ₂ 20	1.0	0.75	Myocardial infarction	0	0	0	
11	M	45	26	11	5	V ₂ 26	1.0	0.2	Myocardial infarction	0	0	0	
12	M	48	10	5	5	V ₂ 20	0.5	0.75	Myocardial infarction	0	0	0	
13	M	58	15	12	4	V ₂ 20	1.5	2.0	Myocardial infarction	0	0	0	
14	M	46	10	7	6	V ₂ 30	1.5	1.0	Myocardial infarction	0	0	0	
15	M	57	15	14	4	V ₂ 17	1.5	0.75	Myocardial infarction	0	0	0	
16	M	42	22	10	5	V ₂ 22	1.5	2.0	Myocardial infarction	0	0	0	
17	M	52	8	6	6	V ₂ 20	1.5	1.5	Myocardial infarction	0	0	0	
18	M	61	16	12	6	V ₂ 16	1.5	3.0	Myocardial infarction	0	0	0	
19	F	78	15	13	6	V ₂ 15	0.25	0.25	Myocardial infarction	0	0	0	
20	M	63	9	3	5	V ₂ 15	2.5	0.5	Myocardial infarction	0	0	0	
21	M	37	14	5	4	V ₂ 20	2.0	1.0	Myocardial infarction	0	0	0	Bilateral hydrothorax
22	M	68	10	9	5	V ₂ 13	1.0	1.0	Myocardial infarction	0	0	0	Ascites
23	M	29	16	13	4	V ₂ 40	0.5	0.75	Myocardial infarction	0	0	0	Left hydropneumothorax
24	M	64	11	7	5	V ₂ 25	0.1	0.1	Myocardial infarction	0	0	0	Hydrothorax and ascites
25	M	46	20	5	5	V ₂ 23	1.5	0.1	Myocardial infarction	0	0	0	Bilateral hydrothorax
26	M	65	8	8	8	V ₂ 25	1.0	0.1	Myocardial infarction	0	0	0	Bilateral hydrothorax
27	M	58	15	5	8	V ₂ 25	1.5	1.0	Myocardial infarction	0	0	0	Hydrothorax and ascites

TABLE IV. MEASUREMENTS OF RS, P, AND T DEFLECTIONS IN TENTHS OF A MILLIVOLT—CONT'D

CASE	SEX	AGE	RS V ₄	RS V ₅	RS V ₆	LARGEST RS DEFLECTION	P	T	CLINICAL DIAGNOSIS	PLEURAL OR PERICARDIAL EFFUSION OR ASCITES	CONGESTION OR EDEMA OF THE LUNGS	PERIPHERAL EDEMA	OTHER CLINICAL FEATURES
51	F	22	5	5	4	V ₂ 8	2.0	0.5	Tuberculous pericarditis	—	0	0	Pneumohydropericardium and pneumohydrothorax
52	M	52	11	7	4	V ₂ 10	1.5	0.1	Constrictive pericarditis	—	—	—	Bilateral hydrothorax and ascites
53	M	52	12	7	4	V ₃ 15	0.1	0.1	Constrictive pericarditis	—	—	—	Hydrothorax and ascites
54	M	54	6	6	5	V ₁ 18	0.5	0.5	Hodgkin's disease (mediastinal)	—	0	0	Massive left hydrothorax
55	M	56	9			V ₂ 17	0.6	0.5	Foreign body in ventricular wall	—	0	0	Hydrothorax and hydropericardium
56	M	41	9	10	7	V ₃ 23	1.5	0.1	Rheumatic heart disease; mitral stenosis	—	—	—	Bilateral hydrothorax
57	M	59	22	18	7	V ₄ 22	0.0	0.1	Rheumatic heart disease; mitral stenosis	—	—	—	Hydrothorax, right; auricular fibrillation
58	M	64	13	7	4	V ₄ 13	1.2	1.0	Metastatic carcinoma to heart and pericardium	—	—	0	Hydrothorax, right; carcinoma of trachea
59	F	36	11	10	4	V ₄ 11	1.75	0.10	Idiopathic hypertrophy	0	0	0	Bronchial asthma
60	F	20	4	7	5	V ₂ 8	1.5	0.75	Idiopathic hypertrophy	0	0	0	Psychoneurosis, neurocirculatory
61	M	47	12	11	4	V ₄ 12	1.5	2.5	Pulmonary emphysema	0	0	0	asthenia
62	F	31	9	7	4	V ₄ 9	1.0	1.0	No heart disease	0	0	0	Carcinoma of stomach
63	M	55	6	10	9	V ₂ 17	0.7	0.5	No heart disease	0	0	0	Parosymmal tachycardia
64	F	53	9	5	4	V ₂ 12	1.75	1.0	No heart disease	0	0	0	
65	M	30	15	9	2	V ₂ 17	0.75	0.75	No heart disease	0	0	0	

In many instances the deflections were very large in some leads although small in one or more of the others. In twenty-nine of the sixty-five cases the largest RS deflection was 2.0 mv or more, and in one case it was 4.0 millivolts. The largest deflection occurred in Lead V_2 in twenty-seven cases, in Lead V_3 in eighteen cases, in Lead V_4 in fourteen cases, in Lead V_1 in three cases, and in Lead V_5 in three cases. This is in contrast to the usual finding in normal persons, where the mean amplitude of RS tends to increase from Lead V_1 to V_4 . This shift of the largest deflection toward the right (from Lead V_4 to V_2) suggests that the electrical axis was rotated from its normal position toward the sagittal plane.

PHYSIOLOGIC CONSIDERATIONS

Wilson pointed out in 1930, in a discussion of the factors theoretically capable of leading to a reduction in the amplitude of the electrocardiographic deflections, that such reduction might be accomplished in one or more of three ways:

1. By conditions that affect the efficiency of the myocardium itself, preventing it from developing an electromotive force of normal magnitude.
2. By conditions that alter the electrical conductivity of the tissues surrounding the heart.
3. By conditions that alter the direction of the mean electrical axis of the heart, thereby changing the size of its projection upon any given lead.

These three principles will be developed more fully later in this paper, when the various types of conditions that were found to be associated with low voltage in this series are discussed.

Conditions Affecting the Total Electromotive Forces Developed by the Myocardium.—Under this heading we shall discuss in particular myocardial infarction and arteriosclerotic heart disease. Myocardial infarction was the most common cardiac abnormality in both groups shown in Table III; it was present in forty-three of one hundred cases in Group A and in thirty-five of the sixty-five cases in subgroup B. To understand how this condition may give rise to low voltage it is instructive to compare a normal precordial electrocardiogram with those from typical cases of myocardial infarction.

The precordial leads of a healthy young man of 30 years are shown in Fig. 1,A. An R wave is present in all leads; it is relatively small in Lead V_1 and grows progressively larger in the leads from points farther to the left until it attains its maximum voltage of 2.1 mv in Lead V_4 ; it then becomes smaller again in Lead V_5 , and in Lead V_6 it is only 1.2 millivolts. The S wave is relatively large in Leads V_1 , V_2 , and V_3 , then rapidly diminishes until in Lead V_6 it is merely vestigial.

Fig. 1,B, represents the precordial electrocardiogram of a 46-year-old physician who had had an acute coronary occlusion five days before it was taken. It is entirely typical of anteroseptal myocardial infarction. In contrast to the normal record, A, the R wave is completely absent in Leads V_1 , V_2 , and V_3 and is only rudimentary in Lead V_4 . In each of these leads there is now only a deep

QS wave, reflecting the negative potential of the ventricular cavity which is transmitted passively through the electrically inert infarcted muscle. The fifth and sixth precordial positions were apparently somewhat lateral to the infarct and the still-healthy myocardium beneath them produced a positive potential as shown by the emergence of the R waves in Leads V_5 and V_6 , but the infarcted area was close enough to transmit some cavity negativity to the exploring electrode; moreover, the positivity previously contributed by the adjacent now-infarcted muscle has been withdrawn, with the result that these R waves did not attain their usual size. The RS-T elevation and late inversion of the T waves complete the electrocardiographic picture of recent infarction. The standard limb leads and unipolar extremity leads are shown in Fig. 1, C. They exhibit unusually small deflections but show no diagnostic features.

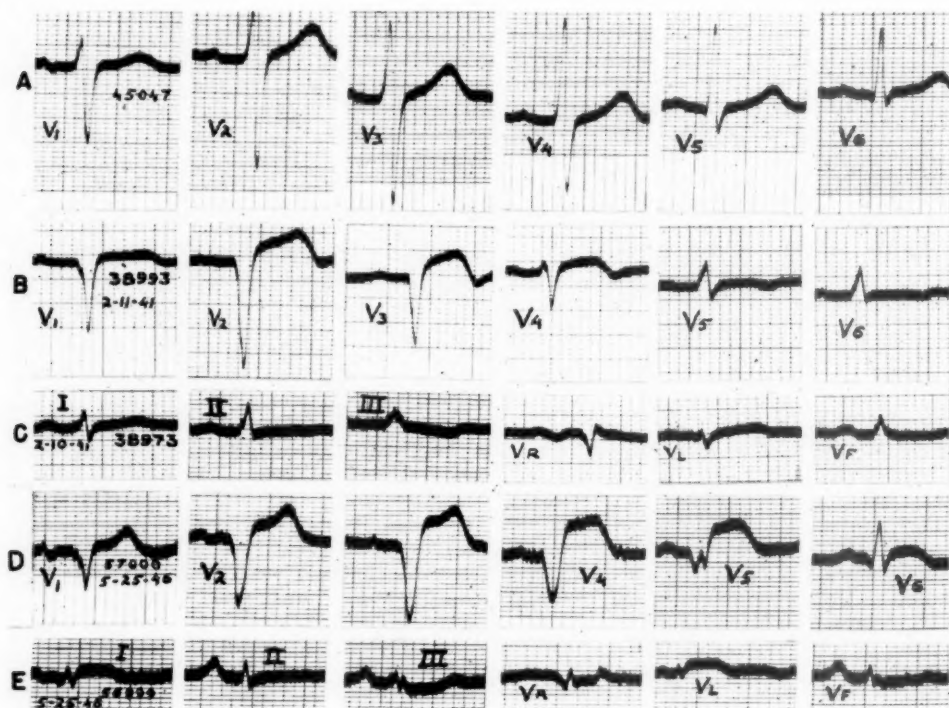


Fig. 1.—A, Normal precordial electrocardiogram. B, Precordial electrocardiogram of patient with recent anterior myocardial infarction, showing low voltage in Leads V_5 and V_6 . C, Low voltage in limb leads; same patient as in B. D and E, Electrocardiogram of another patient with anterior infarction, showing low voltage in Leads V_5 and V_6 and in the limb leads.

Fig. 1, D, represents the precordial electrocardiogram in another typical case of anterior myocardial infarction. The patient, a 63-year-old man, had had a coronary occlusion ten days before this record was taken. The precordial leads are very similar to those in the previous case, showing absence of the R waves and deep QS waves in Leads V_1 , V_2 , V_3 , and V_4 . In Lead V_5 the Q wave

is still present but is not very deep, and a small upward deflection that barely reaches the base line represents the R wave produced by surviving muscle under the exploring electrode. Lead V_6 shows a tiny Q wave also, but this lead was far enough lateral to the main area of infarction to have an R wave 7 mm. tall. The standard limb leads are shown in Fig. 1, *E*. In these the QRS complexes are small in all leads, reflecting the low amplitudes of Leads V_5 and V_6 ; there is a small Q wave in Lead I with upward displacement of RS-T and terminal inversion of the T wave. There is S-T depression in Lead III. The deflections in the unipolar extremity Leads V_R , V_L , and V_F are very small.

In both cases it will be seen that while the deflections in Leads V_5 and V_6 and in the limb leads are small, the deflections in Leads V_2 and V_3 are well within the normal range of amplitude. Because these leads from the right and mid-precordium are influenced chiefly by forces acting in the sagittal plane, they have little relationship to the limb leads. The latter lie in the frontal plane and are accordingly more likely to resemble Leads V_5 and V_6 .

Fig. 2 is particularly instructive as an example of conditions that may lead to a definite increase in QRS amplitude in certain precordial leads while at the same time producing a decrease in others and in the limb leads. It shows serial

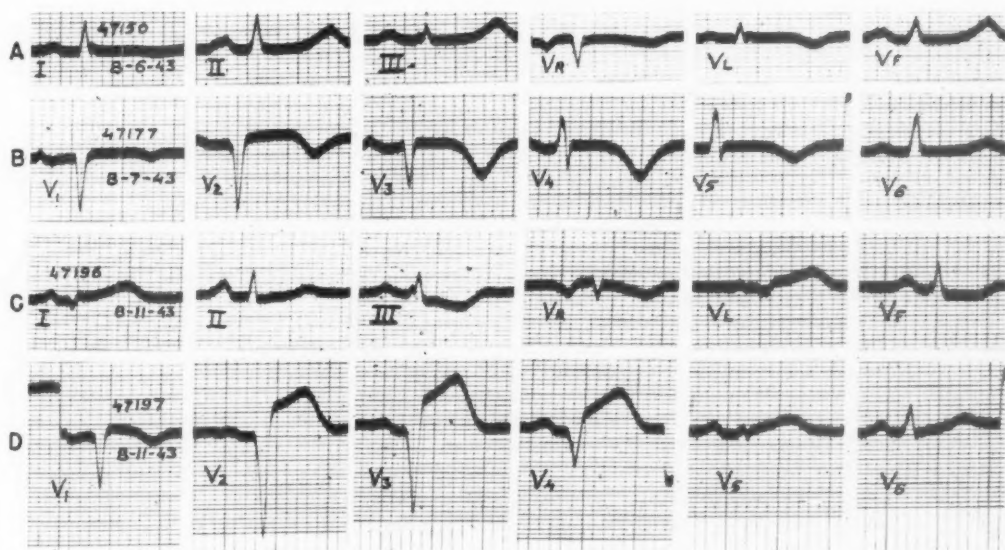


Fig. 2.—A and B, Electrocardiogram taken within twenty-four hours after the patient had had a small anterior infarct. C and D, Electrocardiogram of same patient four days later. With extension of the infarcted area, there has been an increase in the size of the deflections in Leads V_2 and V_3 but a decrease in Leads V_5 and V_6 and in the limb leads.

curves of a 41-year-old woman who had been known to have hypertensive and arteriosclerotic heart disease for some time. On Aug. 6, 1943, she had a sudden attack of severe persistent substernal pain. The standard limb leads shown in Fig. 2, *A*, were taken a few hours later and the precordial leads, *B*, the next day. The precordial leads indicate a small anteroapical infarct; they show complete

absence of the R wave in Lead V_2 , an embryonic R wave in Lead V_3 , and deep inversion of the T waves in Leads V_2 , V_3 , V_4 , and V_5 . The patient continued to have pain, and it is most interesting to compare the first set of records described with those taken four days later, Aug. 11, 1943. In the case of the latter, Lead I, C, shows a Q wave not previously present and reduced QRS amplitude. The precordial leads, D, show changes suggesting that there has been a lateral extension of the infarct. The R wave, previously absent in Lead V_2 only, is now absent in Leads V_1 , V_2 , V_3 , and V_4 . The amplitude of the QS wave in V_2 and V_3 is much greater than it was on August 7, whereas in Leads V_5 and V_6 and in the limb leads the QRS amplitude has become distinctly smaller. The reason for these rather paradoxical changes is that because of the wider extent of infarcted and therefore electrically inert muscle, more of the cavity negativity was transmitted to the electrodes in the C_1 and C_2 positions, and hence the (negative) amplitude in these leads is greater than it was when the infarct was smaller. Leads V_5 and V_6 are affected in the opposite way. Being lateral to the actual infarct, they tend to have positive R waves derived from the surviving healthy muscle underlying the exploring electrode. These R waves do not, however, attain their previous amplitude, partly because some of the forces formerly contributing to them had originated in muscle subsequently infarcted, and were accordingly abolished, and partly because the wider transmission of cavity negativity through the more extensive infarct tends to neutralize those that remain. The limb leads, subject to the same influences as Leads V_5 and V_6 , were likewise reduced in amplitude with extension of the infarct.

The examples we have presented have all been from cases of anterior infarction, but it can be shown that posterolateral infarction may affect the limb leads and the leads from the left precordium in similar fashion.

We have pointed out that anterior infarction very frequently leads to low voltage in Leads V_5 and V_6 , but it is not our intention to suggest that it invariably does so or that when it does it is necessarily accompanied by low voltage in the limb leads. For example, the tracings shown in Fig. 3, A and B, are those of a patient with anteroseptal infarction. The precordial leads, B, show all the characteristic QRS changes and yet the deflections of Leads V_5 and V_6 and of the limb leads, A, are of normal amplitude. Lead V_4 , it is true, shows low voltage. Fig. 3, C and D, represents the limb and precordial leads from another case of anterior infarction. In this case Leads V_4 and V_6 do indeed show low voltage, and yet the deflections in the limb leads are quite large. These two cases are included to show how variable are the combinations that can occur in the different leads, and it is emphasized again that while we have indicated certain general relationships between the QRS amplitudes in Leads V_5 and V_6 and those in the standard leads, it is with full realization that these relations are not always present.

Arteriosclerotic Heart Disease: This is another diagnosis which occurred frequently among the cases in this series (Table III). The term does not have a very precise significance and is often used in cases in which the heart does not show any gross abnormality when examined post mortem. On histologic ex-

amination, however, the myocardium may exhibit extensive streaky and patchy replacement of the muscle by fibrous tissue. Each muscle fiber thus replaced represents the loss of a functioning unit normally contributing to the total electromotive force developed by the heart, and the elimination of a large number of such units may well lead to a pronounced reduction in the size of the electrocardiographic deflections through its effect on the mass of the cardiac muscle. An autopsy was performed in only one of the cases of our series falling into this category. Diffuse fibrosis and scarring of the myocardium was found. A pulmonary infarct was also present in this instance.

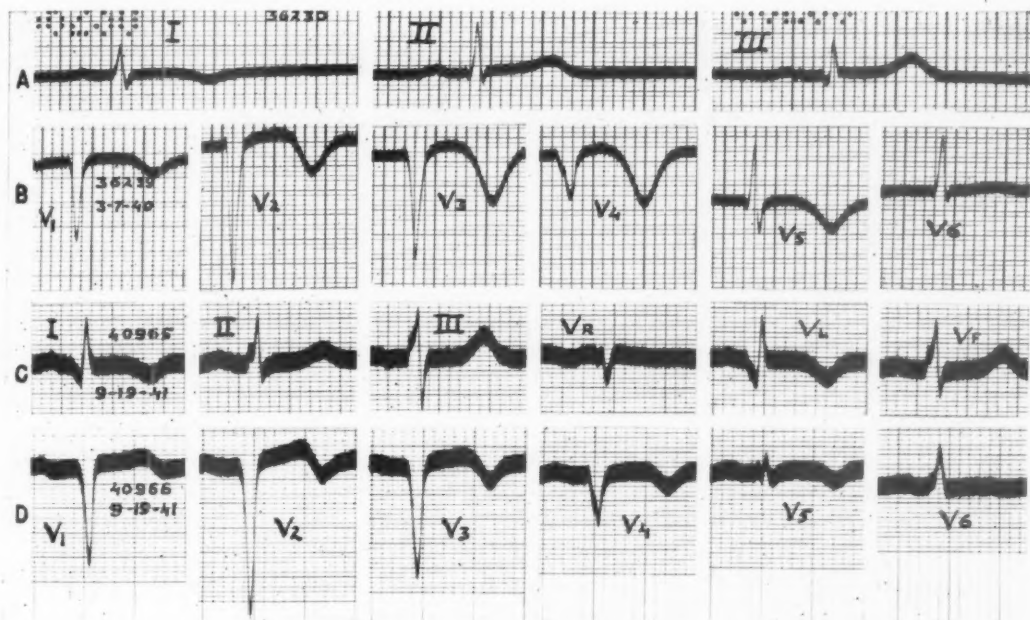


Fig. 3.—A and B, Electrocardiogram of a patient with an anterior infarct, showing normal voltage in Leads V_5 and V_6 and in the limb leads. C and D, Electrocardiogram of another patient with an anterior infarct, showing low voltage in Leads V_5 and V_6 but normal voltage in the limb leads.

Conditions That Affect the Conductivity of the Tissues Surrounding the Heart.—

It will be seen from Table III that after exclusion of the thirty-five cases of myocardial infarction there remain thirty instances of low voltage in one or more precordial leads. In twelve of these the patient had a pleural or a pericardial effusion. There were also six examples of pronounced pulmonary congestion or edema of the lungs, one of marked pulmonary emphysema, and one instance of peripheral edema alone in this group. A number of experimental studies have a bearing upon the manner in which these conditions tend to produce low voltage, even in the absence of primary heart disease.

Eyster and associates²² found that when extensive edema was produced in animals by infusion of the tissues with isotonic salt solution, a conspicuous fall in total body impedance was recorded under certain experimental conditions.

In their impedance experiments, however, these writers employed alternating currents of a frequency (4×10^4 cycles per second) far above any of those found in the electrocardiogram. The bearing of this work upon the impedance offered by the tissues to currents of electrocardiographic frequency is therefore open to serious question. In the experiments of Katz and co-workers,²³ parts of the heart surface were short-circuited by means of lead or tinfoil, or insulated, by means of glass and rubber. Both of these procedures naturally reduced the voltage of the electrocardiogram. Since the conductivity of metals on the one hand and of dielectrics, such as glass or rubber, on the other are of an order entirely different from that of tissue or tissue fluid, such experiments probably have little practical bearing on the problems under consideration here.

Theoretically, an increase in the amount of extracellular fluid might be expected to reduce the voltage of the electrocardiogram by its short-circuiting effect upon the cardiac currents, since such fluid, compared to organized tissues, offers a relatively low resistance to low-frequency current. Kaufman and Johnston²⁴ in experiments on animals measured the specific resistances of the tissues surrounding the heart and found values approximately as follows for the different tissues (expressed in ohms per cubic centimeter): muscle, 575; liver, 506; lungs (normal inspiration), 744; lungs (superinflated), 1,227; pericardium, 405; serum, 98; blood, 185; fat, 1,808.

In the healthy individual the tissues chiefly concerned are pericardium, muscle, liver, and normally inflated lung, and the differences in specific resistance between these tissues are sufficiently small to justify the assumption that the cardiac currents are distributed in accordance with the principles that govern current flow in a homogeneous volume conductor.²⁹ Since the specific resistance of serum is only 98 ohms per cubic centimeter, it is probable that collections of fluid near the heart, whether in the form of massive effusion into the pericardial or pleural spaces or of abnormal extracellular accumulations in the alveoli or connective tissue of the lungs (as, for example, in pulmonary congestion or pulmonary edema), have a more or less pronounced short-circuiting effect upon the cardiac currents and reduce the potential variations recorded at the body surface.

On the other hand, air-containing spaces, such as are present in pneumopericardium and pneumothorax, must act as insulators and would be expected to diminish the size of the electrocardiographic deflections in some leads if not in all. In severe emphysema the lung tissue is thin, atrophic, and relatively avascular and the alveolar spaces are abnormally large, so that it may be that in this condition the pulmonary resistance approaches that for superinflated lung, with consequent insulating effect. It must be conceded, however, that without more accurate knowledge of the actual magnitude of the changes in specific resistance that occur under these various circumstances it is difficult to estimate their effects upon the electrocardiogram with any pretense to accuracy.

The smallest precordial deflections observed in our series occurred in the electrocardiogram of a 22-year-old girl with tuberculous polyserositis. This patient had effusions of fluid into the pericardial and left pleural spaces. When the two upper records of Fig. 4 were taken Feb. 24, 1939, both of these had been aspirated and replaced with air. Roentgenographic examination February 23

had been reported as showing air and fluid in the pericardial sac, with marked thickening of the pericardium, and air and fluid in the left pleural space. The QRS deflections in the limb leads were very small (Fig. 4,A), but those of the precordial leads were even smaller. This is the sole instance in which the precordial deflections were smaller than those of the limb leads. The explanation appears to be that the combination of fluid, air, and thickened pericardium interposed between the chest electrodes and the precordium, with the short-circuiting effect of the one added to the insulating effect of the other, largely prevented the transmission of the potential variations of the cardiac surface to

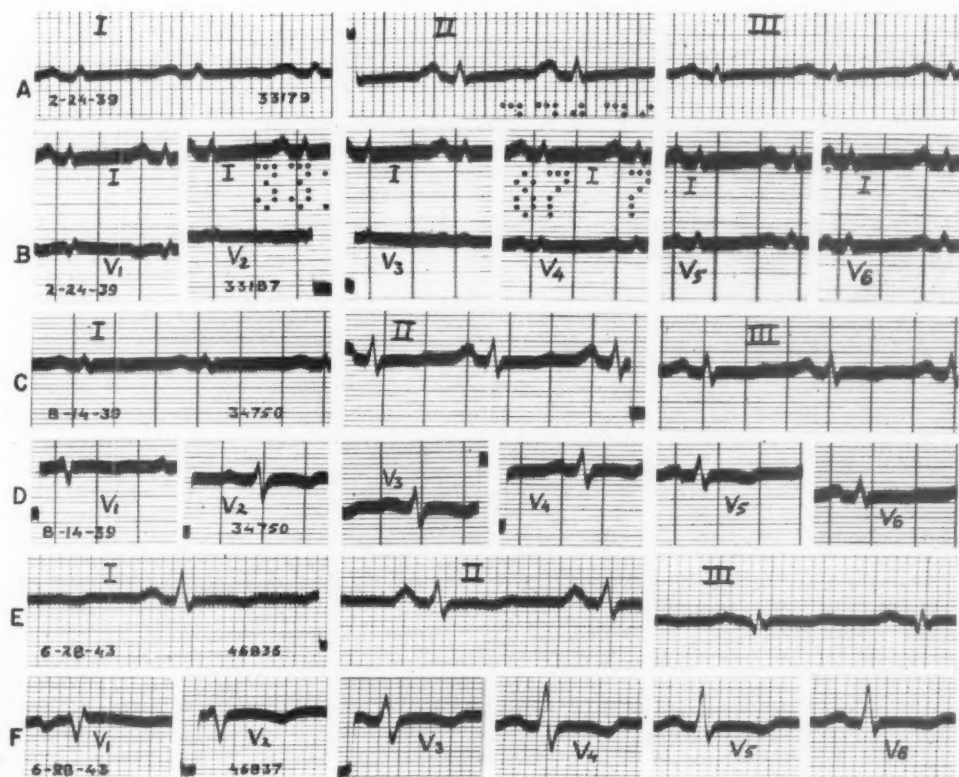


Fig. 4.—Electrocardiograms of a young woman with hydropneumopericardium of tuberculous origin. A and B, Extremely low voltage, especially in the precordial leads, in the presence of air and fluid in the pericardial sac. C and D, Increased voltage after absorption of air from pericardial space; fluid still present. E and F, Further increase in voltage after absorption of fluid.

the precordial electrodes. It is interesting that the smallest deflections occurred in Leads V_2 and V_3 , possibly because with the patient in the supine position the enclosed air lay just beneath the part of the precordium from which these leads were taken. Apparently, the potential variations of the sides and back of the heart were better transmitted to the body surface, for the deflections in Leads V_5 and V_6 and in the limb leads were somewhat larger.

The standard and precordial leads taken Aug. 14, 1939, are shown in Fig. 4, *C* and *D*. Roentgenograms taken on this date show that the air but not all of the fluid had been absorbed from the pericardial sac and that the left hydro-pneumothorax was still present. The deflections of the standard limb leads are seen to have increased moderately and those of the precordial leads considerably, although both are still decidedly subnormal in size.

The two lowermost records in Fig. 4, *E* and *F*, were taken June 28, 1943. Roentgenograms on this date showed the lungs completely expanded and no air or fluid in the pericardial sac. The pericardium itself, however, was 5 to 8 mm. thick, and the roentgenkymogram showed diminished cardiac pulsations. Both limb and precordial leads showed a further increase in the size of the ventricular deflections, but it may be that the extreme thickness of the pericardium still prevented these deflections from attaining normal amplitudes.

Low Voltage With no Pathologic Changes in the Heart or Neighboring Structures.—In our main group of one hundred cases there were six and in the subgroup four patients with no evidence of heart disease, emphysema, or hypothyroidism who were not obese and had no increase in extracellular fluid. In the four last-mentioned cases the clinical diagnoses were (1) minimal pulmonary tuberculosis, arrested; (2) adenocarcinoma of the stomach; (3) neurocirculatory asthenia; (4) no disease. The last two cases will be discussed in detail below. As to the manner in which low voltage is produced in such cases, we can offer only some speculations which leave much to be desired.

The size of the deflections in the standard limb leads depends not upon the total electromotive force generated by the myocardium but upon the projection of this electromotive force, considered as a vector, upon the frontal plane. This component is large when the spatial electrical axis is nearly parallel and small when it is nearly perpendicular to this plane. Otto²⁶ demonstrated this experimentally by rotating the heart forward on a basal transverse axis. He found that the deflections in the limb leads were largest when the apex was most caudad and became progressively smaller as the apex was tilted anteriorly and cephalad. They were smallest when the long axis of the heart was perpendicular to the frontal plane.

Meek and Wilson²⁷ rotated the canine heart about its longitudinal and antero-posterior axes and produced marked alterations in the position of the cardiac electrical axis. In this way they obtained either pronounced left or pronounced right axis deviation with corresponding variations in the size of the ventricular deflections.

Cohn and Raisbeck²⁸ used another approach to the same problem. Instead of displacing the heart itself, they ingeniously rotated the apices of the "Einthoven triangle," and therefore the directions of the standard limb leads, through 360 degrees in the frontal plane. By this method they were able, both in the case of subjects with normal and those with hypertrophied hearts, to obtain tracings depicting either extreme right or extreme left axis deviation.

These and other experiments indicate that position of the cardiac electrical axis and the size of the deflections in the limb leads are determined, to a large

extent, by such factors as the position of the heart and the contour, symmetry, and thickness of the chest wall. In certain cases similar factors probably explain the occurrence of unusually small deflections in the precordial electrocardiograms of subjects who show no other evidence of disease. Thus low voltage is common in Leads V_3 or V_4 when these are from points in the transitional zone where the potential variations of one ventricular surface tend apparently to cancel those transmitted from the other.

There are cases, however, in which most or all of the precordial leads exhibit low voltage, and it is not easy to explain exactly how this happens. Two cases in our series fall into this category. Both displayed unusual features in addition to the low voltage and presented some initial diagnostic difficulties.

CASE 1.—T. M., a young woman, 31 years of age, complained of palpitation, dizziness, vague pains in the chest, choking sensations, and a feeling that she could not get enough air at each breath. There was no history of rheumatic or scarlet fever and there had been no dyspnea or edema. Physical examination was entirely negative; the body habitus was asthenic, the blood pressure 12/88, the heart sounds normal. There was no edema, no pulmonary congestion, no emphysema, no evidence of hypothyroidism. The teleroentgenogram was normal. The final diagnosis was psychoneurosis and neurocirculatory asthenia. The electrocardiogram is shown in Fig. 5. The upper record shows the standard limb leads and unipolar extremity potentials. Low voltage is present in all these leads and the T wave is rather flat in Lead I. The precordial leads are shown in the middle record. The RS deflection is rather small in all leads; it is largest in Lead V_4 , in which it measures only 1.0 millivolt. There is inversion of the T wave in Leads V_1 , V_2 , and V_3 . Inverted T waves are commonly found in Lead V_1 in normal persons and occasionally in Lead V_2 , but after early childhood they are very uncommon in Lead V_3 . The lower record shows the precordial leads after the administration of amyl nitrite. The T wave has become diphasic in Lead V_2 and upright in Lead V_3 , without a conspicuous change in heart rate.

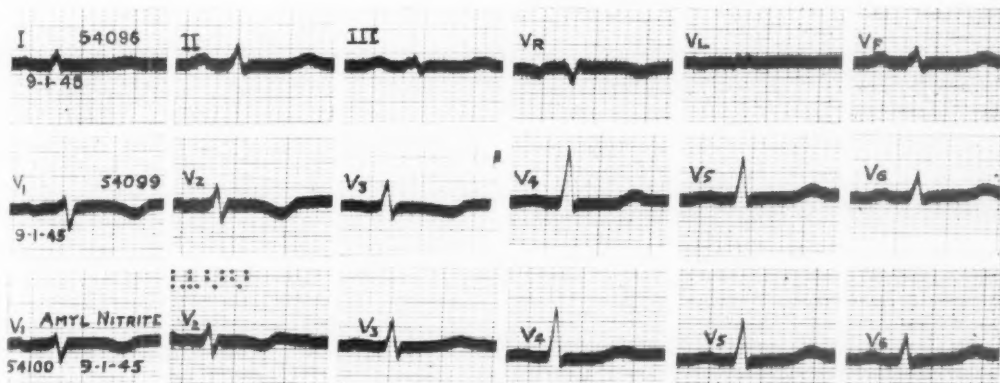


Fig. 5.—Electrocardiogram of a young woman with neurocirculatory asthenia, showing low voltage in almost all leads, flat T waves in Lead I, and inverted T waves in Leads V_2 and V_3 . Lowest record shows tendency for T waves to become upright in Leads V_2 and V_3 after administration of amyl nitrite.

Inversion of the T wave in both the standard and precordial leads in cases of neurocirculatory asthenia, with reversion of the electrocardiogram to normal after the administration of ergotamine tartrate or of amyl nitrite, has been the subject of several recent studies.³⁰ It was of particular importance to recognize the benign nature of the T-wave changes in this case, for the combination of

low voltage and inverted T waves in the electrocardiogram of a patient with complaints referred to the cardiovascular system might have led to an erroneous and mischievous diagnosis of serious heart disease with resulting intensification of the cardiac neurosis already present.

CASE 2.—C. B., an Army medical officer, 30 years of age, was thought by his associates to be somewhat cyanotic about the lips and nail beds while he was testifying before a medical review board. Apart from the tension and anxiety natural to the situation, there were no subjective symptoms. He had always been strong and healthy, of athletic habits and physique; there was no history of rheumatic or scarlet fever or of diphtheria. There had been no undue dyspnea or chest pain, nor indeed was the cyanosis ever noted again. Physical examination and a teleroentgenogram showed no abnormalities and no further attention would have been paid to the episode had it not been for the electrocardiogram, which showed low voltage in the standard limb leads with inverted T waves in Lead I (Fig. 6, *A*). The precordial leads (Fig. 6, *B*) show normal voltage in Leads V_1 , V_2 , V_3 , and V_4 but low voltage in Leads V_5 and V_6 . The QRS complexes are of normal configuration, and the low voltage in the standard limb leads and in the leads from the left precordium, with normal voltage in the remaining precordial leads, could have resulted merely from a shift in the direction of the mean electrical axis toward the sagittal plane, in the absence of heart disease. The inverted T waves in Leads I, V_3 , V_4 , V_5 , and V_6 , however, also required explanation. Fig. 6, *C* shows the effect of exercise on these T waves in Leads V_4 and V_5 . The control record was taken with the subject standing; Leads V_4 and V_5 show inverted T waves as previously. The same leads were then recorded, with the subject again in the upright position, but immediately after he had stepped briskly up and down a standard two-step stairway fifty times. In this record the T waves in Leads V_4 and V_5 are upright. Five minutes later a third record was taken, and the T waves in these leads were again both negative.

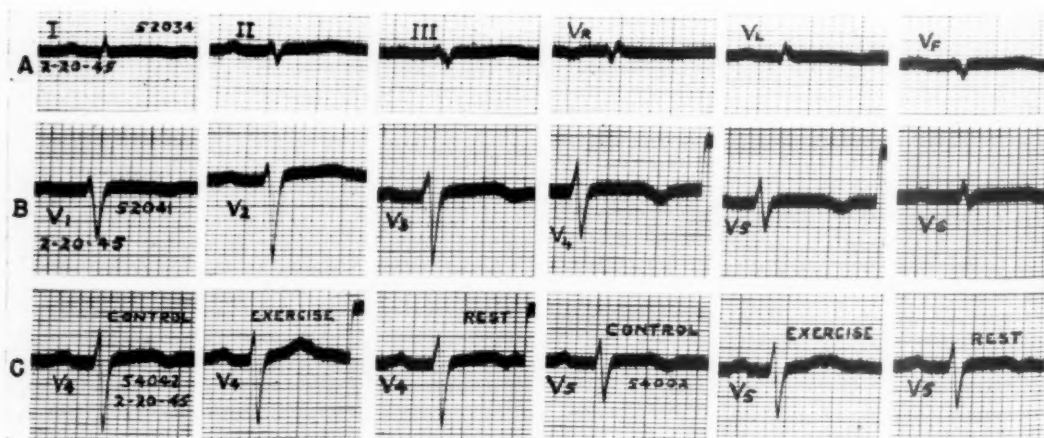


Fig. 6.—Electrocardiogram of an apparently healthy young man. *A*, Low voltage and flat T waves in the limb leads. *B*, Low voltage in Leads V_5 and V_6 and inverted T waves in Leads V_3 , V_4 , and V_5 . *C*, Effect of exercise: T waves in Leads V_4 and V_5 become upright immediately after exercise and then revert to negativity with rest.

As in the previous case, the inconstant T-wave inversion was regarded not as a sign of disease but as a physiologic variant apparently related in some way to an unstable balance between sympathetic and vagal tonus. Whether or not this conclusion was correct is uncertain; the patient's health two years after the electrocardiographic peculiarity was first noted is still excellent.

Low Voltage of P and T Waves.—In a paper already referred to, Wilson²¹ suggested that the QRS deflections might be low in the electrocardiograms of some normal persons because the electrical forces produced by one part of the heart were neutralized by those arising in other parts. In this case, he reasoned, the P wave and perhaps the T wave should be of normal amplitude. On the other hand, when the QRS deflections were diminutive because of altered tissue conductivity or myocardial degeneration, then the P and T deflections should also be small.

In this study the P and T deflections were classified as showing low voltage if both were less than 0.1 mv in amplitude in all three of the standard limb leads. In our total group of one hundred cases with low voltage of QRS in the limb leads, small P and T deflections occurred in thirty patients. Thirteen of the patients concerned had hydrothorax or hydropericardium and twelve had marked congestion of the lungs with or without peripheral edema. The remaining five had no extracellular fluid accumulations.

DISCUSSION

Several conclusions are suggested by an analysis of our cases and the comparison of our data with those collected by other investigators.

1. The electrophysiologic factors that produce low voltage in the standard limb leads tend to produce low voltage in the precordial leads also. This might be expected *a priori*, but certain authors¹⁴ were led to the conclusion that, with few exceptions, no conditions other than severe myocardial disease produced low voltage in the precordial leads. Our own series, like theirs, is biased by the method of sampling used, for most of the subjects included in it must have been suspected of having myocardial disease before the electrocardiogram was ordered. It is not surprising, therefore, that most of them did have serious organic disease. Nevertheless, a certain number were found not to have heart disease and some had no organic disease of any kind.

2. It is very uncommon to find extremely low voltage in all six precordial leads even in the presence of extensive disease. Most often, when the deflections in the standard limb leads are small, those of the leads from the left side of the precordium are also small, since both reflect forces acting in the frontal plane. The forces acting in the sagittal plane may actually be very large in some of these cases, and this is suggested by the occurrence in some instances of large deflections in leads from the midprecordium, such as Leads V_2 and V_3 . These sagittal forces are almost without effect upon the standard limb leads.

3. In the diagnosis of myocardial disease the configuration of the QRS deflections is of far greater significance than their size.

SUMMARY AND CONCLUSIONS

1. Low voltage occurred in one or more of precordial Leads V_2 to V_6 in sixty-five of one hundred cases selected because of the occurrence of low voltage in the limb leads.

2. Low voltage occurred in all six precordial leads in three cases only. It was most frequent in Lead V_6 (fifty-six cases) and least frequent in Lead V_2 (three cases).

3. In most instances in which certain leads showed low voltage, the size of the deflection of other leads was well within normal limits, and in many the chief deflection in the lead in which the voltage was largest was distinctly greater than the average for its kind. The largest deflection occurred most often in Lead V_2 in contrast to the normal situation in which it is most frequent in Lead V_4 . This suggests that in our series the mean electrical axis, on the average, was shifted toward the sagittal plane.

4. By far the greater proportion of the patients in this series had serious heart disease. Myocardial infarction was present in thirty-five and arteriosclerotic heart disease in fifteen of the sixty-five cases. The manner in which these conditions may produce low voltage in certain leads is discussed in the text.

5. Low voltage did occur, however, in both precordial and limb leads of some patients with no intrinsic disease of the heart. Most of these had extracardiac disorders of a type that would be expected to change the electrical conductivity of the tissues surrounding the heart.

6. Low voltage also occurred in both standard limb leads and precordial leads of a small number of persons who exhibited no evidence of physical disease. In such cases it is probably the result of an unusual orientation of the anatomic and hence of the mean electrical axis of the heart.

The writer wishes to express his gratitude to Dr. Frank N. Wilson for his many valuable suggestions and for his help in the preparation of this paper.

REFERENCES

1. Sprague, H., and White, P. D.: Significance of Electrocardiograms of Low Voltage, *J. Clin. Investigation* **3**: 109, 1926.
2. Hepburn, J., and Jamieson, R. A.: Prognostic Significance of Several Electrocardiographic Abnormalities, *AM. HEART J.* **1**: 623, 1926.
3. Master, A. M., and Pardee, H.: Effect of Heart Muscle Disease on the Electrocardiogram, *Arch. Int. Med.* **37**: 42, 1926.
4. Willis, F. A., and Killins, W. A.: Electrocardiograms of Low Voltage, *Arch. Int. Med.* **40**: 332, 1927.
5. Turner, K. B.: Low Voltage in the Electrocardiogram, *Arch. Int. Med.* **50**: 380, 1932.
6. Barrit, A. S.: Clinical Significance of Electrocardiograms With Low Voltage QRS Groups in the Presence of Normal T-Waves, *Brooklyn Hosp. J.* **2**: 147, 1940.
7. Crawford, J. R.: Findings in 1,000 Routine Electrocardiograms, *Proc. Life. Ext. Exam.* **1**: 14, 1939.
8. Johnson, H. J.: Incidence of Electrocardiographic Changes by Age Among 2,400 Males, *Proc. Life Ext. Exam.* **2**: 88, 1940.
9. Graybiel, A., McFarland, R. A., Gates, D. G., and Webster, F. A.: Analysis of the Electrocardiograms Obtained From 1,000 Healthy Young Aviators, *AM. HEART J.* **27**: 524, 1944.
10. McFarland, R. A., Graybiel, A., Liljencrantz, E., and Tuttle, A. D.: Analysis of the Physiological and Psychological Characteristics of 200 Civil Airline Pilots, *J. Aviation Med.* **10**: 160, 1939.
11. Stewart, C. B., and Manning, G. W.: A Detailed Analysis of the Electrocardiograms of 500 RCAF Aircrew, *AM. HEART J.* **27**: 502, 1944.
12. Larsen, K., and Skulason, T.: The Normal Electrocardiogram. 1. The Analysis of the Extremity Derivations From 100 Normal Persons Whose Ages Ranged from 30 to 50 Years, *AM. HEART J.* **22**: 625, 1941.
13. Shipley, R. A., and Halloran, W. R.: The Four-Lead Electrocardiogram in 200 Normal Men and Women, *AM. HEART J.* **11**: 325, 1936.

14. Bellet, S., and Kershbaum, A.: The Significance of Low Voltage of the QRS Complex in the Precordial Leads, *AM. HEART J.* **22**: 195, 1941.
15. Chamberlain, E. Noble, and Hay, J. D.: The Normal Electrocardiogram, *Brit. Heart J.* **1**: 105, 1939.
Master, A. M.: The Precordial Lead in 104 Normal Adults, *AM. HEART J.* **9**: 511, 1933.
Robinson, R. W., Contratto, A. W., and Levine, S. A.: The Precordial Lead, *Arch. Int. Med.* **63**: 711, 1939.
Katz, L. N., and Kissin, M.: A Study of Lead IV: Its Appearance Normally, in Myocardial Disease, and in Recent Coronary Occlusion, *AM. HEART J.* **8**: 595, 1933.
Roth, I. R.: On the Use of Chest Leads in Clinical Electrocardiography, *AM. HEART J.* **10**: 798, 1935.
16. Leach, C. E., Reed, W. C., and White, P. D.: Low Voltage of the QRS waves in the Electrocardiogram, With Especial Reference to Lead IV, *AM. HEART J.* **21**: 551, 1941.
17. American Heart Association and Cardiac Society of Great Britain and Ireland: Joint Recommendations of the Committees on Standardization of Precordial Leads, *AM. HEART J.* **15**: 107, 1938.
Committee of the American Heart Association for the Standardization of Precordial Leads: Supplementary Report, *AM. HEART J.* **15**: 235, 1938.
18. Kossmann, C. E., and Johnston, F. D.: The Precordial Electrocardiogram. 1. The Potential Variations of the Precordium and of the Extremities in Normal Subjects, *AM. HEART J.* **10**: 925, 1935.
19. Wilson, F. N., Johnston, F. D., MacLeod, A. G., and Barker, P. S.: Electrocardiograms That Represent the Potential Variation of a Single Electrode, *AM. HEART J.* **9**: 447, 1934.
20. Bryant, Marion: Distribution of Myocardial Action Currents, M. S. Thesis, University of Virginia, submitted September, 1946.
21. Wilson, F. N.: The Distribution of the Potential Differences Produced by the Heart Beat Within the Body and At Its Surface, *AM. HEART J.* **5**: 599, 1930.
22. Eyster, J. A. E., Maresh, F., and Krasno, M. R.: The Nature of the Electrical Field About the Heart, *Am. J. Physiol.* **106**: 574, 1933.
23. (a) Katz, L. N., and Korey, H.: The Manner in Which Electric Currents Generated by the Heart Are Conducted Away, *Am. J. Physiol.* **111**: 83, 1935.
(b) Katz, L. N., Sigman, E., Gutman, I., and Ocko, F. H.: The Effect of Good Electrical Conductors Introduced near the Heart on the Electrocardiogram, *Am. J. Physiol.* **116**: 343, 1936.
24. Kaufman, W., and Johnston, F. D.: The Electrical Conductivity of the Tissues Surrounding the Heart and Its Bearing on the Distribution of the Cardiac Currents, *AM. HEART J.* **26**: 42, 1943.
25. Wilson, F. N., Johnston, F. D., Cotrim, N., and Rosenbaum, F. F.: Relations Between the Potential Variations of the Ventricular Surfaces and the Form of the Ventricular Electrocardiogram in Leads From the Precordium and the Extremities, *Tr. A. Am. Physicians* **56**: 258, 1941.
26. Otto, H. L.: The Effect of Altering the Position of the Heart on the Voltage of the Electrocardiogram, *Proc. Soc. Exper. Biol. & Med.* **26**: 204, 1928.
27. Meek, W. J., and Wilson, A.: The Effect of Changes of Position of the Heart on the QRS Complex of the Electrocardiogram, *Arch. Int. Med.* **36**: 614, 1925.
28. Cohn, A. E., and Raisbeck, M. J.: An Investigation of the Relation of the Position of the Heart to the Electrocardiogram, *Heart* **9**: 311, 1922.
Cohn, A. E., and Raisbeck, M. J.: On the Relation of the Position of the Enlarged Heart to the Electrocardiogram, *Heart* **9**: 331, 1922.
29. Wilson, F. N., MacLeod, A. G., and Barker, P. S.: The Distribution of the Action Currents Produced by Heart Muscle and Other Excitable Tissues Immersed in Extensive Conducting Media, *J. Gen. Physiol.* **16**: 423, 1933.
30. Wendkos, M. H.: The Influence of Autonomic Imbalance on the Human Electrocardiogram: 1. Unstable T-Waves in Precordial Leads From Emotionally Unstable Persons Without Organic Heart Disease, *AM. HEART J.* **28**: 549, 1944.
31. New York Heart Association, Criteria Committee: Nomenclature and Criteria for Diagnosis of Diseases of the Heart, New York Heart Association, Inc., 1945.

WEIGHT OF THE RED BLOOD CORPUSCLES IN HEART FAILURE DETERMINED WITH LABELLED ERYTHROCYTES DURING AND AFTER DECOMPENSATION

G. NYLIN, M.D., AND S. HEDLUND, M.D.
STOCKHOLM, SWEDEN

IN DETERMINING the volume of the circulating blood, one can, in principle, employ substances which display a particular affinity either for blood corpuscles or for plasma. Dyes are an especially useful example of the latter variety of substance and were first introduced for this purpose by Keith, Rowntree, and Geraghty in 1915.¹ Recently blue azo dye, T-1824, has been most frequently employed, the method having been devised by Dawson, Evans, and Whipple² in 1920. This dye has been used in particular by Gibson and Evans³ in their clinical studies. It is injected into the circulation and its concentration is then determined colorimetrically in samples of blood. The concentration curve presents two phases: in the first phase there is a rapid fall in concentration during the first three to six minutes (the mixing curve); the second phase consists of a more gradual fall in concentration (the disappearance slope). Equilibrium is considered to exist at the point where the first phase merges into the second. In fifteen normal cases, Gibson and Evans found that equilibrium was reached seven and one-half minutes after the injection of the dye, whereas Gregersen,⁴ who has used this method to study many problems of the circulation, found the corresponding time to be nine minutes. The plasma volume is obtained by extrapolating from the point of equilibrium to the zero level. The mixing curve is due to the mixing of the dye with the blood, while the disappearance slope has been found to depend on the fact that blue azo dye, which is adsorbed on the serum albumin, diffuses out into the tissues and is partially removed by the reticulo-endothelial system. In 1940, Cardozo⁵ showed that fifteen to thirty minutes after the injection of the dye into the blood stream the lymph began to acquire a blue color and that two hours after injection the concentration of the dye in the lymph was 40 per cent of its concentration in the plasma. The choice of a point of equilibrium is thus arbitrary. The volume of the circulating blood corpuscles is calculated from the hematocrit reading and the plasma volume. The method has been freely criticized, most recently by King, Cole, and Oppenheimer⁶ and by Gregersen and Rawson.⁷

The method in which the cellular volume is determined first differs in principle from the dye method which we have just discussed. In 1882, Gréhant

From the Second Medical Clinic, Sabbatsberg's Hospital.
Received for publication Sept. 6, 1946.

and Quinquaud⁸ introduced carbon monoxide for this purpose in experiments on animals. The method has since been modified for clinical use on various occasions by Salvesen,⁹ Haldane and Smith,¹⁰ van Slyke and Robscheit-Robbins¹¹ and Asmussen.⁴⁷ Most of the investigators who have made use of the carbon monoxide method have had the subject breathe in a closed system for varying periods: Haldane and Smith,¹⁰ for two to three minutes; Arnold, Carrier, Smith, and Whipple,¹² for four minutes; McIntosh,¹³ Steinmann,^{14,15} Plesch,¹⁶ and Grosse-Brockhoff and Molineus,¹⁷ for about nine minutes; and Chang and Harrop¹⁸ for as many as twenty minutes. Blood samples were then taken and their carbon monoxide content determined either by the van Slyke method of gas analysis or by Haldane's carmine titration method, with a spectrometer, or by the photoelectric method of von Hartmann¹⁹ and Steinmann.¹⁴ Van Slyke and Robscheit-Robbins¹¹ have employed another method; they have injected blood saturated with carbon monoxide intravenously and have then determined by gas analysis the concentration in samples taken four minutes later. Most of the investigators mentioned estimate the margin of error at about 5 per cent.

The carbon monoxide method has been criticized on the following grounds, among others. Since carbon monoxide is a poison, its concentration in the blood must be kept very low in cases of cardiac insufficiency or anemia. The purity of the carbon monoxide must be determined before inspiration. The amount of carbon monoxide remaining in the closed system, which is estimated at 1 to 2 per cent, must also be taken into account. Steinmann¹⁴ has also pointed out that the blood carbon monoxide in habitual smokers may range between 0 and 5 per cent, and, must, therefore, be determined before the experiment. The patient must take an active part in the experiment; this may be difficult in cases of cardiac insufficiency. A very important consideration is the fact that a certain amount of the carbon monoxide, estimated at 5 per cent, is taken up by the myoglobin and leaves the blood stream. Haldane and Smith¹⁰ have also drawn attention to another small source of error: the fact that 0.3 per cent carbon monoxide can be physically dissolved in blood. For all of these reasons, the blood carbon monoxide tends to fall, and one cannot obtain a reliable equilibrium level. The calculated volume of the blood corpuscles, therefore, tends to be too high.

Smith, Arnold, and Whipple²⁰ carried out comparative determinations of the blood volume in dogs with Welcker's method, the carbon monoxide, and the blue azo dye method and found that the plasma method gave the largest blood volume, whereas the Welcker and the carbon monoxide methods gave approximately the same results. These authors also have discussed the principle of the hematocrit and have expressed the view that its reading is too high when the blood sample is taken from the jugular vein, the reason being that the proportion of plasma to blood corpuscles varies in vessels of different caliber. Stead and Ebert²¹ state that a hematocrit reading of 40 to 50 for the jugular vein is about 25 per cent higher than the cellular volume obtained by direct determination, as, for example, by the carbon monoxide method. Similar views have been expressed by Hahn, Ross, Bale, Balfour, and Whipple²² and by Fåhræus.²³ By comparing the circulating blood volume, as determined by the plasma method and hemato-

crit, with the volume as determined by the carbon monoxide method and hematocrit, Bazett, Sunderman, Maxfield, and Scott²⁴ and others have found that the former method gave the larger figure. These investigators, as well as Smith, Arnold, and Whipple,²⁰ recommend a combination of the carbon monoxide and plasma methods for determining the circulating blood volume.

The introduction of radioactive isotopes appears to have provided a method for determining the volume of circulating blood corpuscles in which mixing with the blood is rapid and equilibrium is maintained for fifty to sixty minutes with radioactive phosphorus (according to Nylin) or for weeks with radioactive iron (according to Hahn, Bale, and Balfour²⁵). Hevesy and associates²⁶⁻²⁸ have devised an excellent method of labelling the red blood corpuscles with radioactive phosphorus, with the help of which Nylin,³⁰⁻³² and Nylin and Malm²⁹ have carried out a number of clinical investigations. Nylin has pointed out that it is important to observe the process of dilution by means of repeated tests during a considerable period. When the dilution curve is known, it is possible to determine in any particular case at what point equilibrium is established and to calculate the volume of the circulating blood. This method also enables one to carry out valuable investigations during the period in which equilibrium is maintained. Nylin and Malmström³³ and Gernandt and Nylin³⁴ have previously measured the circulation time with decholin and have found that the prolonged circulation time and the persisting sensation of taste in compensated patients with dilated hearts are closely correlated with the amount of residual blood in the heart. Nylin has since verified this by using red blood corpuscles labelled with radioactive phosphorus.

Hevesy, Køster, Sørensen, Warburg, and Zerahn³⁵ have employed similar methods in their physiologic studies on normal subjects. They have compared the volume of circulating blood, as determined with radioactive phosphorus, with that determined by carbon monoxide and have found the latter to be 30 per cent higher, largely because of the action of myoglobin in taking up carbon monoxide. Brown, Hempelmanm, and Elman³⁶ and Hahn and Hevesy^{26,27} have employed another method of determining the blood corpuscular volume in dogs and rabbits, respectively, with radioactive phosphorus. These investigators first inoculate a donor animal and then inject its activated blood into the experimental animal whose blood volume is to be measured. The same procedure has also been used by Anderson.⁴⁶ A donor must also be used when the circulating blood volume is determined with radioactive iron.^{22-25,37-38} The investigators who have employed this method have also found that the cellular volume determined with radioactive iron is about 25 per cent smaller than that determined from plasma volume with blue azo dye and the hematocrit. It thus appears that radioactive isotopes are particularly suitable for determining the volume of circulating blood corpuscles.

Relation of Blood Volume and Heart Failure.—A knowledge of the variations in the blood volume in cases of cardiac insufficiency has been found to contribute to an understanding of the mechanism involved in the development and elimination of decompensation. The fluctuations in blood volume have been correlated

with other clinical observations during the decompensation and after the administration of digitalis. Wollheim³⁹ employed the trypan red method to determine the total volume of blood in a large number of clinical cases and has found the normal value to be 5,330 c.c., or 83.9 c.c. per kilogram of body weight.* The average volume of circulating blood in decompensated patients with edema was found to be 5,890 c.c., or 84 c.c. per kilogram of body weight. The range was from 74 to 120 c.c. per kilogram of body weight. After compensation was restored, this fell to an average value of 4,990 c.c., or 70.0 c.c. per kilogram of body weight. The range was from 56 to 76 c.c. per kilogram of body weight. Ewig and Hinsberg⁴⁰ employed a combination of the carbon monoxide and plasma methods, as well as the carbon monoxide method alone, and found an increase in the blood volume in decompensation (6 to 7 liters). They found that administration of digitalis caused a considerable reduction in volume to approximately the normal value, or approximately 4.5 liters. Gibson and Evans,³ using blue azo dye, observed an increase in both blood and erythrocyte volume in decompensation, the former amounting to between 22 and 50 per cent in the various stages of insufficiency. They observed a reduction in the whole blood volume after compensation was restored in all cases and a reduction in the corpuscular volume in most cases; the former fell about 1 liter, and the latter, in certain cases, about 500 cubic centimeters. They also observed that a reduction in the plasma volume preceded the fall in cellular volume. Plesch,¹⁶ using the carbon monoxide method, also observed an increase in the whole blood volume and total hemoglobin in decompensation, while Schürmeyer⁴¹ and Steinmann,¹⁵ using the same method, found that the increased blood volume fell after administration of digitalis. Seymour, Pritchard, and Longley,⁴² using blue azo dye, observed a 25 per cent reduction in volume after digitalis. Meneely and Kaltreider⁴³ studied fifteen decompensated patients and observed a 46 per cent increase in the whole blood volume and a 48 per cent increase in cell volume. In three patients in whom compensation was restored, they observed a fall in both. Using blue azo dye, Waller and Blumgart⁴⁴ determined the blood volume in five cases of decompensation and found it to be 125 to 220 per cent of the normal. In every case, the volume fell after the restoration of compensation. Ehrström⁴⁵ obtained similar results with congo red. In a previous investigation, Nylin³¹ found that the erythrocyte volume, determined with radioactive phosphorus, fell by 18 per cent when compensation occurred, the corresponding fall in the whole blood volume being 28 per cent.

METHODS

With a view to studying more closely the variations in the volume of the red blood corpuscles during the various stages of decompensation and after its elimination, we determined the volume of the erythrocytes in a number of patients by labelling them with radioactive phosphorus. Clinical progress during administration of digitalis was observed by means of a routine physical examination and determination of weight, diuresis, pulse frequency, circulation time, venous

*The range in these normal cases was from 75 to 85 c.c. per kilogram of body weight.

pressure, and heart volume by x-ray. In addition to repeated estimations of serum protein, phosphatase, citric acid, Takata, serum bilirubin, hemoglobin, and red blood corpuscles, we determined the diameter of the blood corpuscles and their resistance as well as the degree of reticulosis in various stages of cardiac insufficiency.

In this investigation, the corpuscular volume was determined by the method which was employed in previously published work.²⁹⁻³² Following the procedure described by Hahn and Hevesy^{26,27} and Hevesy and Zerahn,²⁸ red blood corpuscles from the patient were activated with 0.03 mc. of radioactive phosphorus by two hours' shaking in a thermostat at 37° C. Four milliliters of the labelled blood (the plasma was, of course, also activated) were injected into a vein in one of the patient's arms. After the injection, samples of venous blood were taken from the other arm at suitable intervals and centrifuged. The activity of the erythrocytes, and sometimes that of the plasma as well, was then determined with Geiger-Müller equipment. The weight of the circulating blood corpuscles was then calculated from the formula $X = A \times B$ where X is the weight of the erythrocytes in grams, A the weight of labelled corpuscles injected, and B the proportional relationship between the specific activity of the injected labelled corpuscles and the average specific activity of the blood corpuscles taken from samples in which equilibrium has been established. In converting the weight of the erythrocytes in grams to their volume in milliliters, the specific gravity of the corpuscles was taken to be 1.08, as given by Hevesy. A fuller account of the procedure and its sources of error was given in previous papers by Hevesy, Zerahn, and Nylin.

The volume of the plasma and of the whole blood in circulation was then calculated from the volume of the erythrocytes and the hematocrit reading. We are fully aware that a hematocrit reading, based on blood taken from an arm vein, does not indicate the true proportion between blood corpuscles and plasma in the circulation as a whole; we have referred to this earlier. The figures which are given for plasma volume and total circulating blood volume are given only for purposes of comparison with earlier investigations.

The hematocrit reading was carried out in accordance with the procedure originally described by Hedin.⁴⁸ The blood samples were centrifuged in capillary tubes at 6,000 revolutions per minute for thirty minutes. Heparin was used as an anticoagulant (Ponder,⁴⁹ Millar⁵⁰). The venous pressure was measured in the manner described by Moritz and Tabora,⁵¹ and the radiologic estimation of the heart volume was determined by the method advised by Liljestrand, Lysholm, Nylin, and Zachrisson.⁵⁰

RESULTS

Nineteen patients, none of whom had any disorder of the blood or circulation, provided material for twenty-one determinations of the normal corpuscular volume and whole blood volume by the method which has been described. Six were healthy men in good training; six patients were being treated for gastric ulcer or gastritis; two patients were given the diagnosis of chronic polyarthritis; one, chronic nephritis; one, spondylosis deformans; one, neurosis; one, acute

pulmonary tuberculosis; and one, acute pleurisy. We found the average weight of the blood corpuscles to be 2,100 grams, or 31.2 grams per kilogram of body weight. The latter figure, 31.2 grams, is lower than the figure of 36.0 grams found by Hevesy, K ϕ ster, S ϕ rensen, Warburg, and Zerahn³⁵ in twenty-two subjects. There was an unmistakable correlation between the weight of the blood corpuscles and the body weight; heavy, muscular patients possess more blood corpuscles than thin ones (Fig. 1).

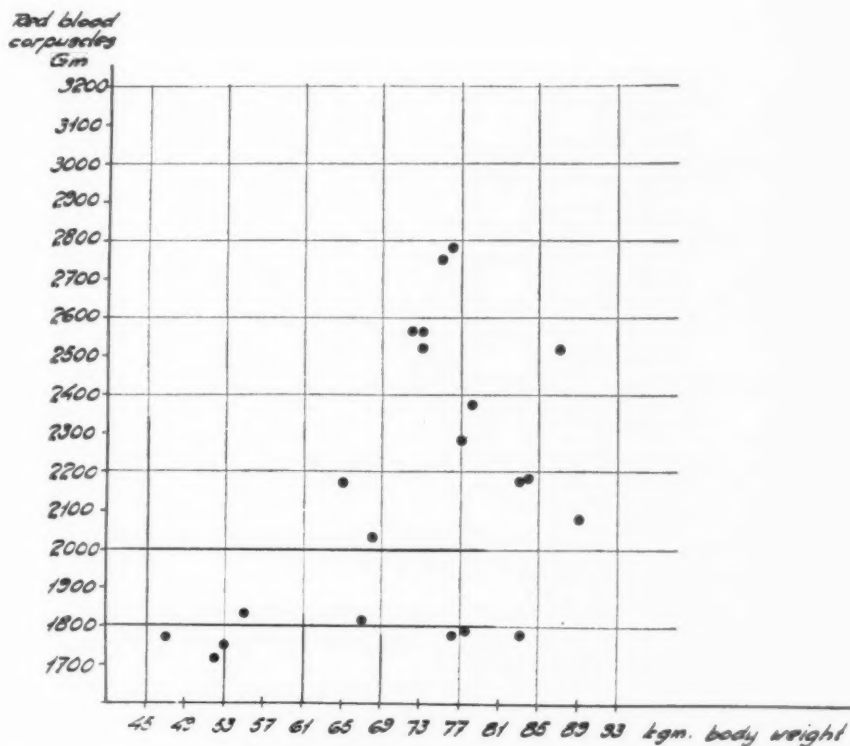


Fig. 1.—Correlation between body weight and the weight of red blood corpuscles in normal cases.

As previously mentioned, Nylin and associates have shown that the circulation time (determined with the decholin method) in cardiac insufficiency indicates not only the degree of congestion, but also, to a large extent, the dilatation of the heart and, therefore, the amount of residual blood remaining in it. Statistical analysis of a large number of cases has shown that there is a definite correlation between the radiologic volume of the heart and the circulation time in compensated cardiac disease. With a view to investigating this matter more closely, Nylin has, as reported in previous papers, measured the circulation time by labelling red blood corpuscles with radioactive phosphorus by the method which has been described. If one studies the dilution curve of the blood of normal individuals after injection of the labelled corpuscles, one finds that the activity is measurable after ten to fifteen seconds, that it reaches a maximum after twenty

to twenty-five seconds, and that equilibrium is established after sixty seconds and maintained for about one hour. There is found to be close agreement between the circulation time determined by the decholin method and that obtained by labelling erythrocytes with radioactive phosphorus. In cardiac cases, on the other hand, the dilution curve is different.

Fig. 2 shows a case of this kind. The patient was a 48-year-old man with mitral stenosis who was completely compensated. The venous pressure was 10.5 cm. and the circulation time, 25 to 79 seconds as determined with decholin. The first sensation of taste was thus delayed and its total dura-

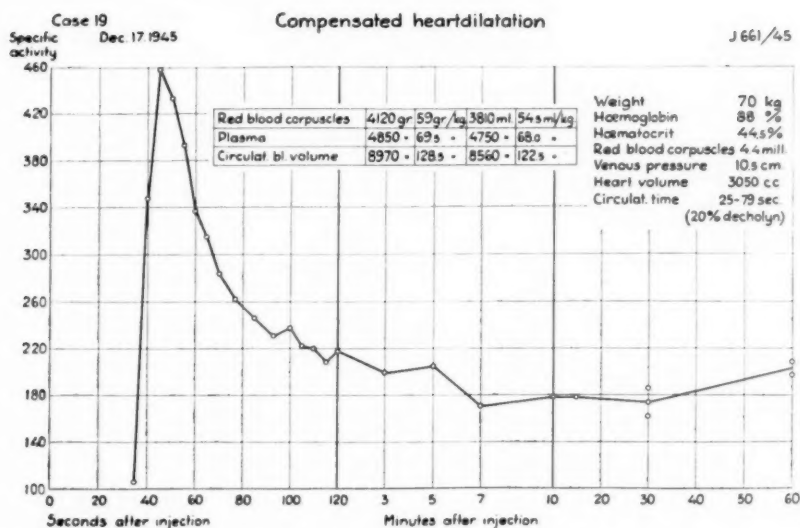
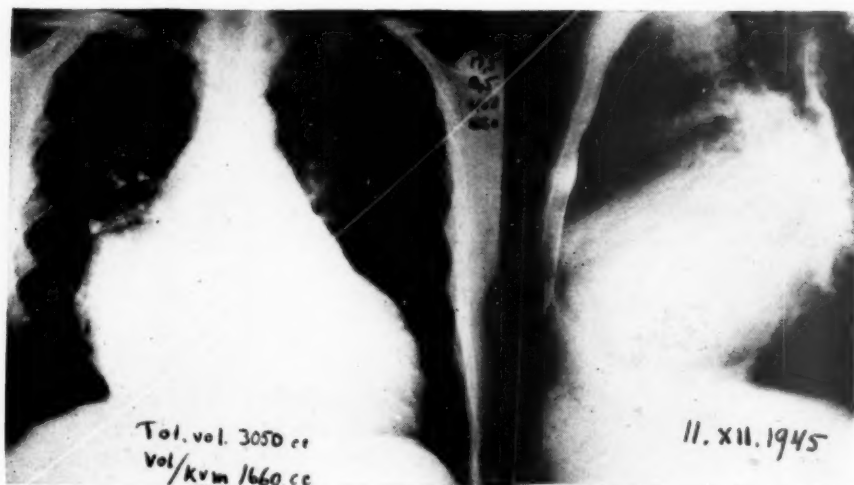


Fig. 2.—Results obtained in a 48-year-old man with mitral stenosis. Equilibrium was not established until seven minutes after injection of the labelled corpuscles. The curve was therefore shifted to the right.

tion prolonged. The heart was very large; its radiologic volume was 3,050 cubic centimeters. The dilution curve, based on the activity of arterial blood, differed clearly from the normal. The first measurable activity was delayed (thirty-five seconds) and the maximum likewise delayed (fifty seconds), and equilibrium was not established until after seven minutes. The whole curve has thus been displaced to the right. Between the thirtieth and sixtieth minute, the patient ate a light meal and took a short walk. The result was an increase of about 10 per cent in the specific activity of double samples taken at the sixtieth as compared with the thirtieth minute. This may have been a true increase due to the fact that some labelled blood had been held up in the dilated heart or in some organ where the circulation was particularly slow and partial stasis had occurred. This labelled blood may have reached the vein from which the samples were taken later than the rest of the labelled blood. We will return to this question later.

Our method involves the activation of both corpuscles and plasma, and we inject this activated blood into the subject without centrifuging away the plasma. This is done because we have found that the activity of the plasma falls very rapidly without affecting the activity of the corpuscles. Fig. 3 is based on an experiment of this kind. It shows that the activity of corpuscles and plasma

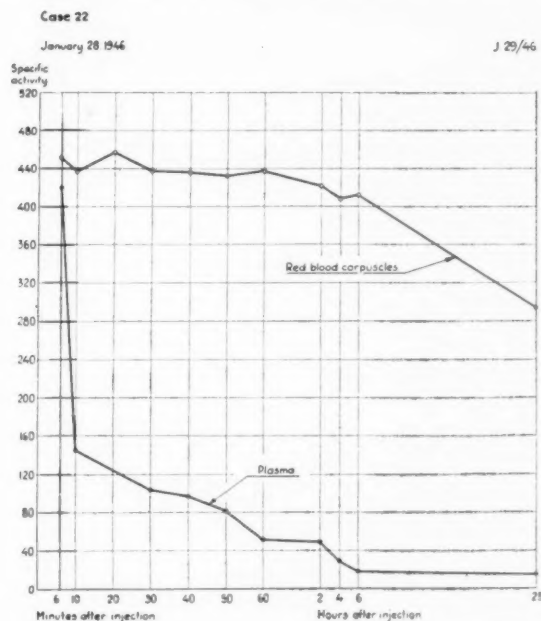


Fig. 3.—Specific activity of red blood corpuscles and plasma during twenty-four hours after intravenous injection of tagged erythrocytes and plasma.

was the same at the end of six minutes. Four minutes later, plasma activity had fallen 65 per cent, and, after sixty minutes, it was only 10 per cent of its original value. The activity of the corpuscles, on the other hand, remained con-

stant throughout. Our procedure involves, therefore, a considerable simplification of the method.

Using the method which has been described, we determined the corpuscular volume and whole blood volume of seven patients in various stages of decompensation and after recovery from it. The patients were also subjected to thorough clinical examinations which included the determination of venous pressure, circulation time, and heart volume.

The diagnoses were as follows: mitral stenosis in three patients, cardiosclerosis in two patients, hypertension in one patient, and aortic regurgitation in one patient.

CASE 21.—A 65-year-old man with cardiosclerosis and auricular fibrillation displayed, on admission, extensive edema and hydrothorax and was severely dyspneic. The venous pressure was 13 cm. H₂O and the heart was considerably dilated (Table I and Fig. 4). The weight of the erythrocytes was found to be 2,820 grams, or 25 grams per kilogram of body weight. This corresponds to 30 grams per kilogram of dry body weight; that is, body weight after elimination of edema. The whole blood weight was 7,550 grams and the plasma weight 4,730 grams. Rest in bed resulted in the loss of 15.6 kilograms of weight and in a fall of venous pressure to 8 centimeters. Examination after rest showed the plasma weight to be 3,850 grams and the whole blood weight 6,680 grams. The reduction is natural in view of the amount of fluid the patient had lost. The corpuscular weight remained the same: 2,830 grams. After further treatment with digitalis, complete compensation was restored and there was a considerable reduction in the volume of the heart (it still remained somewhat dilated) and a fall in the venous pressure to 6 cm. of water. The plasma weight fell to 3,340 grams and the whole blood to 5,600 grams. The corpuscular weight, therefore, was 2,260 grams, or 24 grams per kilogram of dry weight, a reduction of 570 grams, or 20.2 per cent. The change in the proportion of corpuscles to plasma in connection with the removal of fluid is illustrated by the rise in the hematocrit reading from 36 to 40 per cent between the two first estimations, and by the rise of hemoglobin from 70 to 75 per cent and the increase in erythrocytes from 3.6 to 3.9 million. At the third examination, the weight of both erythrocytes and plasma was found to have fallen by about the same amount, but the hematocrit reading remained 40 per cent. The hemoglobin, however, was found to have risen to 79.5 per cent and the red blood corpuscles to have increased to 4.3 million.

A detailed analysis of the various specific activity graphs plotted at different times reveals certain interesting points. Thus, in the examinations on Feb. 11, 1946, and Feb. 25, 1946 (shown in Fig. 4), one sees that the activity of the samples increased during the first ten minutes before becoming fairly constant. This is probably an indication that the labelled blood corpuscles were retained for a short time in the dilated heart before being thrown out into the blood stream. Another remarkable thing is that in the first examination, when the decompensation was most pronounced, the level of activity at the first, second, fourth, and sixth hours was higher than in the earlier examinations. The figure for the twenty-fourth hour is in fact as high as that for the twentieth minute. This persistence of activity at a high level for a number of hours differs considerably from the behavior shown by normal patients. In later studies made when the decompensation was improving, the duration of activity, as shown by the graphs, changed again and approached the normal. Thus in the examination of Feb. 25, 1946 (Fig. 4), one finds that the activity after one, two, and four hours was more or less the same as after the corresponding number of minutes. The small discrepancy that does exist can be explained by the fact that the im-

TABLE I. THE VOLUME OF RED BLOOD CORPUSCLES IN HEART FAILURE BEFORE AND AFTER COMPENSATION

Case	21				22				23				24				25		26	27
Diagnosis	Cardiosclerosis				Aortic regurgitation				Mitral stenosis				Mitral stenosis				Hypertension		Cardiosclerosis	Mitral stenosis
	11. 2.	25. 2.	20. 3.		14. 1.	28. 1.	6. 5.		1. 2.	18. 3.	26. 3.	9. 4.	5. 3.	14. 4.	6. 5.		27. 3.	18. 4.	11. 4.	8. 3.
Cell volume Grams	2,820	2,830	2,260		2,980	2,980	2,290		2,100	1,700	2,060	1,980	2,840	1,960	2,140 2,220		3,010	3,100	2,210 2,200	2,185 2,240
Grams per kilogram	30 (25)	30 (29)	24 (24)		46 (41)	46 (44)	35 (34)		35 (33.5)	28 (28)	34 (34)	33 (33) 6	44 (43)	30 (31)	33 (33) 34 (34)		40.5 (40)	42 (42)	26 26	26 43 (41.5)
Hematocrit	36%	40%	40%		41%	38%	35%		54%	45%	45%	48%	41%	42%	42%		53%	50%	41%	51%
Plasma (Gm.)	4,730	3,850	3,340		4,055	4,600	4,020		1,830	1,970	2,380	2,030	3,850	2,550	2,780 2,890		2,530	2,930	3,000 3,000	2,495 1,960
Blood volume (Gm.)	7,550	6,680	5,600		7,035	7,580	6,310		3,930	3,670	4,440	4,010	6,690	4,510	4,920 5,110		5,540	6,030	5,210 5,200	4,200
Weight loss	1.6 kg	15.6 kg	18.6 kg		0 kg	9 kg	10 kg		1.5 kg	4.5 kg	3.5 kg	4.5 kg	—	1 kg	0 kg		8.3 kg	10.3 kg	—	0.7 kg
Venous pressure (Cm.)	13	8	6		27	13	16		23	10.5	11	7	12.5	16	14		10	6	17	19
Edema	+++	+	—		+++++	+++	+		++	—	—	—	—	—	—		++	—	+	++

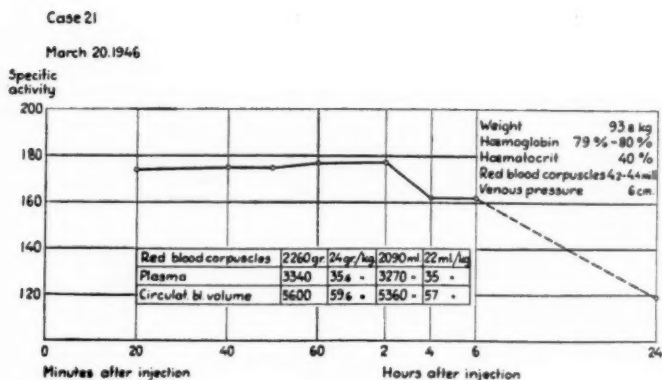
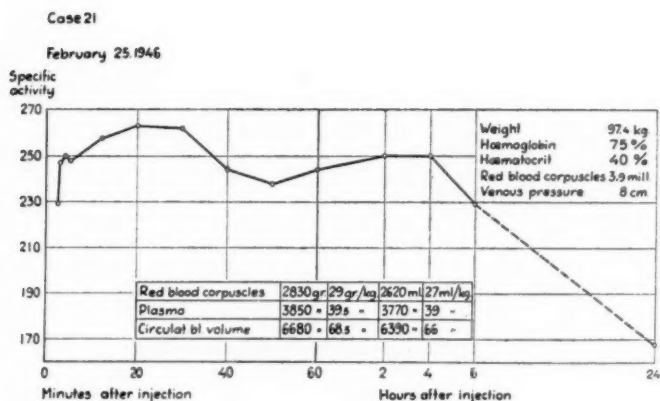
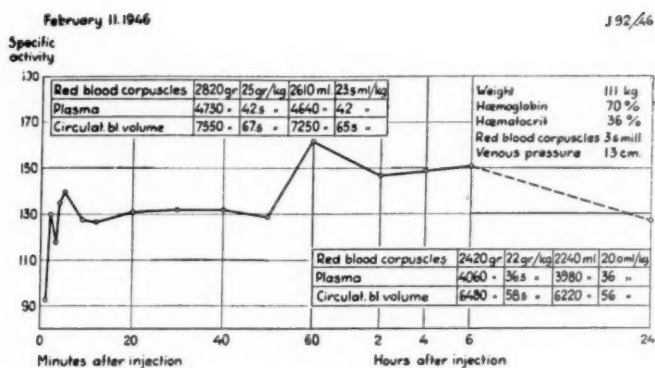


Fig. 4. — Findings in Case 21. See text.

Heart Failure

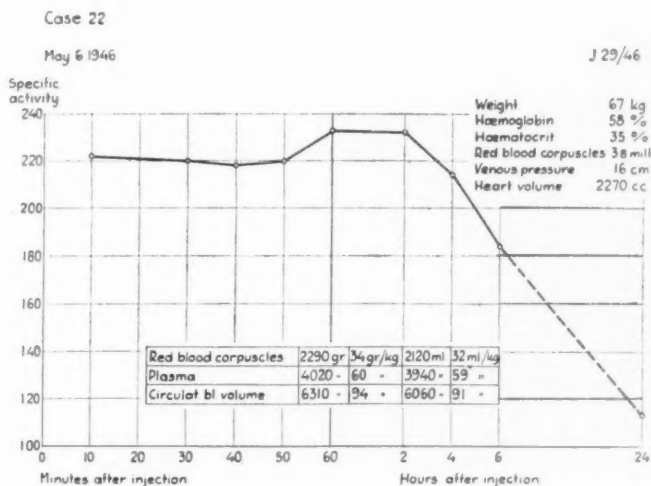
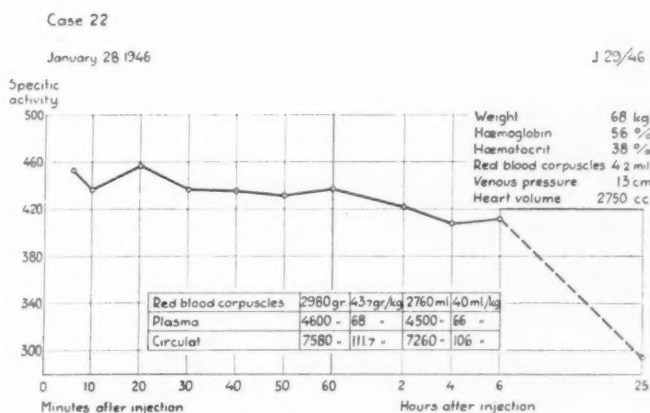
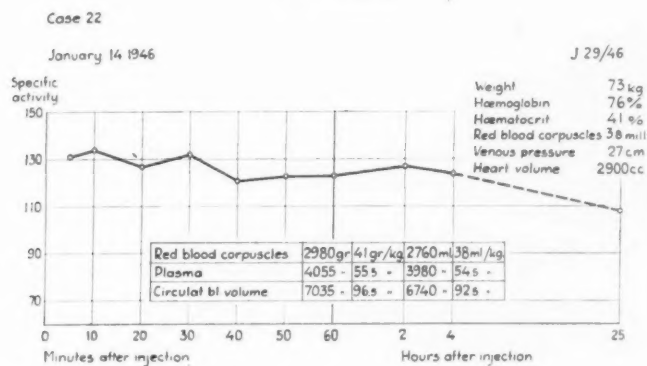


Fig. 5.—Findings in Case 22. See text.

pulses were calculated at a very high level of activity. On this occasion, the figures for the sixth, and particularly the twenty-fourth, hour signify a definite decline. After full compensation was restored, the decline in activity began after two hours. We will return in a later discussion to the interpretation of these interesting phenomena.

CASE 22.—A 68-year-old man with aortic regurgitation and a positive Wassermann had had symptoms of cardiac insufficiency for about eight years (Fig. 5 and Table I). On being admitted to the hospital, he was suffering from severe decompensation with extreme edema, severe cyanosis and dyspnea, hepatomegaly, and a venous pressure of 27 cm. of water. The volume of the heart was 2,900 cubic centimeters. Examination showed the blood corpuscular weight to be 2,980 grams, which was equivalent to 41 grams body weight or 46 per kilogram of dry weight. The plasma weight was found to be 4,055 grams and the weight of the whole blood was found to be 7,035 grams. The decompensation became progressively worse, but incision of the dorsal surfaces of the feet, as described by Nylin and Björck, and intravenous injections of cedilanid resulted in the patient's losing a considerable quantity of fluid and 9 kilograms in weight. The venous pressure was reduced to 13 cm. H₂O and the volume of the heart to 2,750 cubic centimeters. The blood corpuscular weight remained the same, 2,980 grams, but there was an unexpected increase in the plasma and whole blood, the former rising by 545 grams to 4,606 grams. The fall in the hematocrit reading from 41 to 38 per cent and in the hemoglobin from 76 to 56 per cent also indicates that the proportion of cells to plasma underwent a change in the interval between the two examinations. We have previously stressed the fallacy of judging true proportion of blood corpuscles to plasma in the whole circulation by a hematocrit reading based on blood drawn from a vein in the arm. This increase in plasma, therefore, should be treated with reserve.

About three months later, when the patient was in fairly good condition with only slight edema and cyanosis, a venous pressure of 16 cm. H₂O, and the heart volume had diminished to 2,270 c.c., we found that whole blood, plasma, and blood corpuscles had all diminished, the latter by no less than 690 grams to 2,290 grams (equivalent to 35 grams per kilogram of dry weight or 34 grams per kilogram of body weight). The change in the proportion of blood corpuscles to plasma was seen again; the hematocrit reading fell to 35 per cent, the hemoglobin to 58 per cent, and the red blood corpuscles to 3.8 million. In addition to cardiac insufficiency, anemia was present throughout the study. Variations in the anemia were presumed to be due to the change in the amount of blood corpuscles and plasma consequent upon the elimination of the decompensation. The plasma protein was fairly constant throughout at about 7.1 per cent.

The individual graphs show certain features analogous to those mentioned in the previous case. At the height of decompensation, the activity of the erythrocytes remained constant from the fortieth minute to the fourth hour; the activity at the twenty-fourth hour was again remarkably high. As the decompensation improved, there was again a fall in activity, first from the sixth hour and later from the fourth hour. This matter will be discussed later.

CASE 23.—A 32-year-old man with mitral stenosis had had symptoms of cardiac insufficiency for about four years. This patient differed from the previous patients inasmuch as the insufficiency chiefly expressed itself in pulmonary congestion with severe dyspnea and cyanosis and a palpable liver but only slight edema (Table I and Fig. 6). The venous pressure was 23 cm. H₂O, and the volume of the heart 1,750 cubic centimeters. An estimation of the blood corpuscles while the patient was in decompensation showed their weight to be 2,100 grams, equivalent to 33.5 grams per kilogram of body weight or 35 grams per kilogram of dry weight. The whole blood amounts to 3,930 grams and the plasma to 1,830 grams. After compensation, with a fall in the venous pressure to about 10 cm. H₂O and in the volume of the heart to 1,460 c.c., the blood corpuscular weight was found to have remained fairly constant, the figures being 1,700 grams on March 17, 2,060 grams on March 23, and 1,980 grams on April 9, 1946. These figures are equivalent to 28, 34, and 33 grams, respectively, per kilogram of dry weight. The whole blood also remained fairly level, the figures being 3,670, 4,440, and 4,010 grams, respectively.

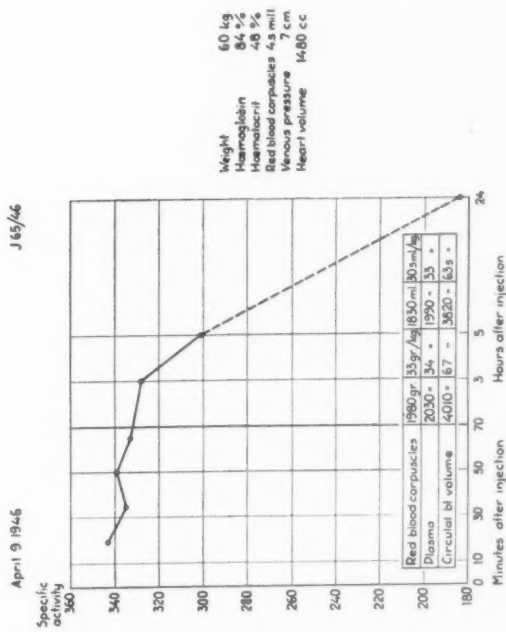
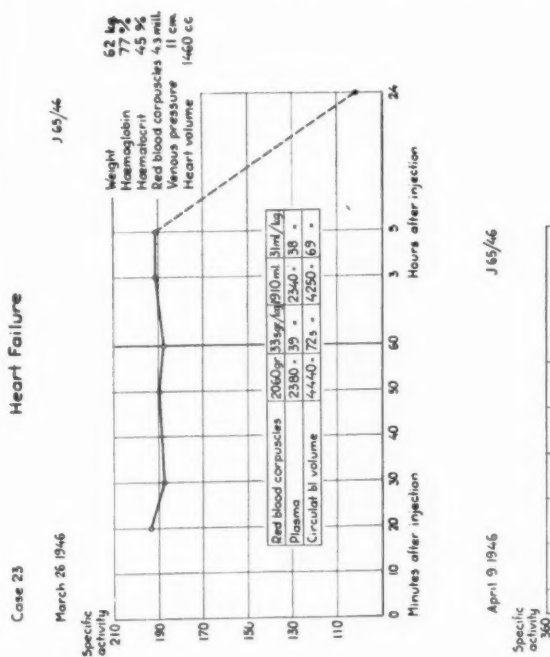


Fig. 6.—Findings in Case 23. See text.

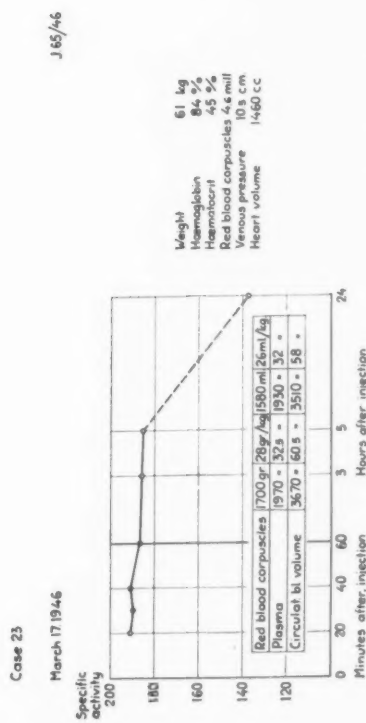
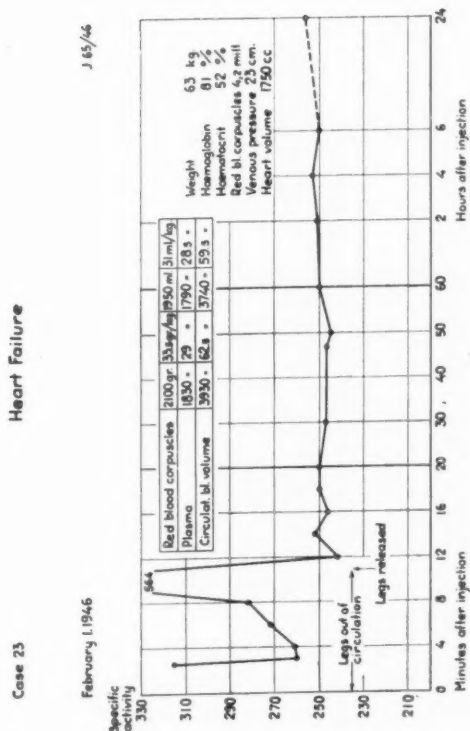


Fig. 7.—Findings in Case 24. See text.

During the examination on Feb. 1, 1946, the lower limbs were occluded for about ten minutes by cuffs applied to the upper part of the thighs and pumped up to a pressure above the systolic pressure. The cuffs were then removed; the activity figures in the later part of the graph, therefore, represent the total volume of circulating blood. In this manner, one can determine the amount of blood in the lower limbs. We will not discuss this matter on this occasion because it will be presented in another paper, but it is worthy of note that in this experiment a considerable number of impulses were recorded just before the cuffs were taken off. This is not easy to explain. A possible explanation is that some of the labelled corpuscles may have been delayed in the dilated heart or in some other organ where the circulation rate is reduced (the liver, for example), and may have been prevented from promptly reaching the faster circulation from which the blood samples were taken. This case also shows that during decompensation the activity of the labelled corpuscles remains constant up to the twenty-fourth hour after injection. After compensation has been established, there is again a steady fall in activity from the fifth hour, and in the final examination from the third hour.

CASE 24.—The patient was a 35-year-old man suffering from mitral stenosis who had had symptoms of cardiac insufficiency for about eight years (Table I and Fig. 7). As in the previous case, the decompensation showed itself in pulmonary congestion with severe dyspnea and a palpable liver, but no edema. The venous pressure fluctuated throughout between 12.5 and 16 centimeters. In the first examination, the corpuscular weight was found to be 2,840 grams, which was equivalent to 44 grams per kilogram of dry weight or 43 grams per kilogram of body weight. The whole blood weighed 6,690 grams and the plasma 3,850 grams. A month later, after treatment with digitalis, the corpuscular weight had fallen to 1,960 grams or 31 grams per kilogram of body weight. The plasma had diminished to 2,550 grams, and the whole blood to 4,510 grams. The reduction in corpuscular weight was, therefore, 880 grams, or 12 grams per kilogram of body weight. After another month had elapsed, the corpuscular weight was found to be practically unchanged; that is, 2,140 and 2,220 grams, respectively, as determined by double injection. The corresponding figures per kilogram of body weight were 33 and 34 grams, respectively. Figures for whole blood were 4,920 and 5,110 grams, respectively. The hematocrit reading was the same throughout, showing that the proportion of blood corpuscles to plasma was constant. The hemoglobin, on the other hand, fell from 80 per cent in the first examination (during decompensation) to 74 per cent in the second and 75 per cent in the third examination.

In the first examination of this case, we made a slight change in the usual routine; the blood samples were obtained by arterial puncture. This gives a dilution graph which shows the progressive mixing of the labelled corpuscles with the blood. As has already been mentioned, cardiac insufficiency causes a change in the appearance of this graph by displacing it to the right in a characteristic manner. In this case, the maximum activity was not reached until the fortieth to forty-fifth second, and equilibrium was not established until the ninth minute. At the sixth minute, the patient moved the arm into which the labelled corpuscles were injected, and the blood samples taken during the subsequent two minutes displayed a considerably increased activity. It is probable that this peak is due to labelled corpuscles having remained at the site of the injection until the active movement of the arm released them into the blood stream.

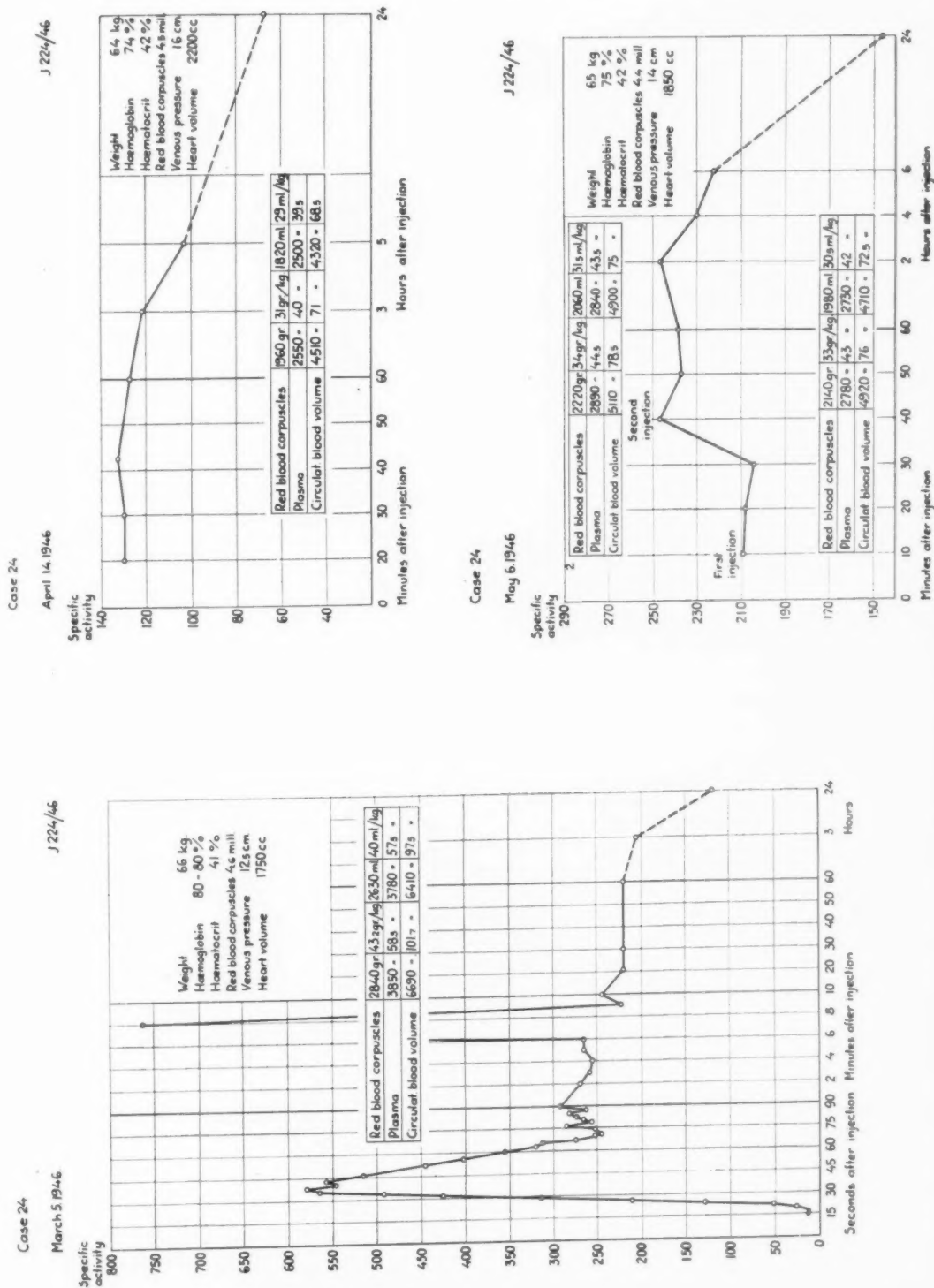


Fig. 7.—Findings in Case 24. See text.

In the examination on May 6, a second injection of labelled corpuscles was given thirty-one minutes after the first, with the result that either of the two parts of the graph can be used in the calculation of the corpuscular weight. This method enables one to make two separate calculations in the course of one examination. The discrepancy between the two determinations in this case is only 80 grams, or 3.6 per cent, showing that the source of error in the method is very small.

CASE 25.—A man with hypertension had had progressive symptoms of cardiac insufficiency for about nine months. He was admitted to the hospital with severe edema and dyspnea, as well as cyanosis (Table I and Fig. 8). Measurement of the heart by x-ray showed its volume to be 1,700 cubic centimeters. Five days later, when the patient had lost 8.3 kilograms in weight, as a result of rest in bed and intravenous injections of cedilanid, and the venous pressure had fallen to 10

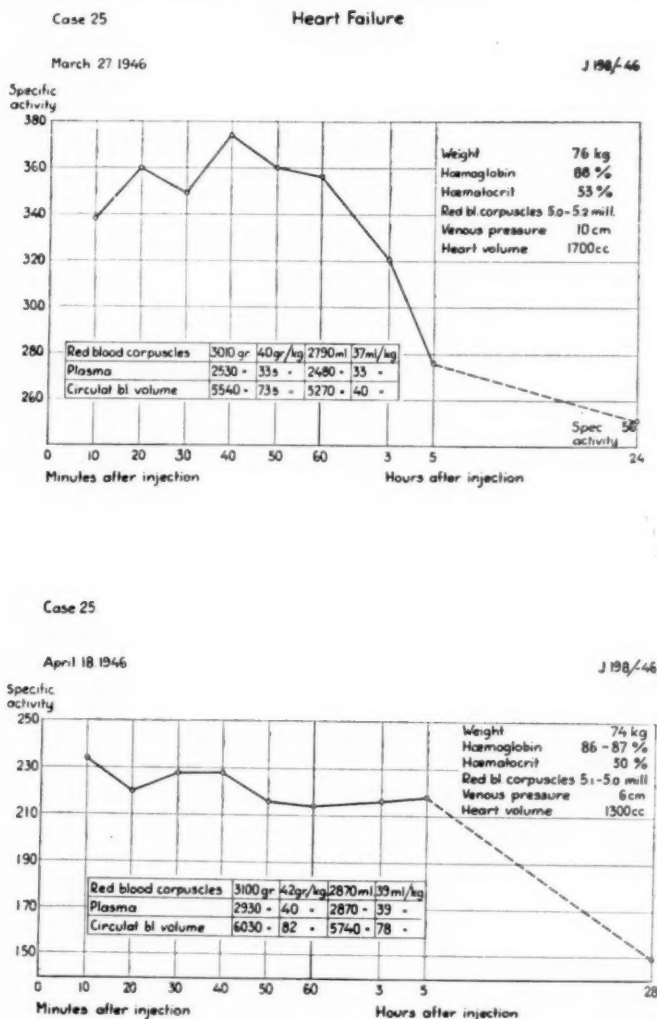


Fig. 8.—Findings in Case 25. See text.

cm. H_2O , the corpuscular weight was found to be 3,010 grams, or 40 grams per kilogram of body weight; the plasma weight 2,530 grams; and the whole blood 5,540 grams. Three weeks later after complete compensation had been restored, and the venous pressure has fallen to 6 cm. and the volume of the heart to 1,300 c. c., another determination showed the weight of the corpuscles to be unchanged: 3,100 grams or 42 grams per kilogram of body weight. Thus there had been no diminution in the quantity of blood corpuscles, which was still large. The whole blood weighed 6,030 grams and the plasma 2,930 grams. Although there had been a further reduction in the edema (about 2 kilograms), there had been, if anything, an increase in plasma. The explanation is perhaps to be sought in the fact that the serum protein had risen from 5.8 per cent in the first examination to 7.2 per cent in the second examination. In addition to the pressure of extracellular fluid, the plasma proteins constitute an important factor in the maintenance of plasma volume. In this case, the hematocrit readings, 53 per cent and 50 per cent, respectively, the hemoglobin, 87 per cent, and the count of red blood corpuscles, 5.1 million, also indicate that there had been an increase in the total quantity of erythrocytes. Fig. 8 shows the graphs based on these two examinations.

CASE 26.—A 50-year-old man suffering from cardiosclerosis had had symptoms of insufficiency, mainly in the form of unpleasant breathlessness, for about one year (Table I and Fig. 9). Examination showed his principal symptoms of decompensation to be dyspnea, cyanosis, and slight edema at the ankles. The venous pressure was 17 cm. H_2O and the heart volume 1,850 cubic centimeters. In the first examination, while there was decompensation, double injections of labelled corpuscles showed the corpuscular weight to be 2,210 and 2,200 grams, respectively, equivalent to 26 grams per kilogram of body weight. Thus, the difference in this estimation was only 10 grams. After being treated for two months, compensation was restored; the volume of the heart had declined to 1,080 c.c. (later the volume declined to 800 c.c.), and the venous pressure had declined to 3.5 cm. of water. Another determination of corpuscular weight by double injections showed it to be unchanged, the figures on this occasion being 2,290 and 2,087 grams, respectively, a difference of only 200 grams. These figures correspond to 27 and 25 grams per kilogram of body weight, respectively. While there was decompensation, the whole blood measured 5,200 grams and the plasma 3,000 grams. After compensation had been restored, the plasma value declined to 2,500 grams, and the whole blood value declined to about 4,700 grams. The rise in the hematocrit reading from 41 to 46 per cent and in the hemoglobin from 56 to 81 per cent also indicated that there has been an increase in the proportion of blood corpuscles to plasma. Fig. 9 shows the graphs of the double injections on both occasions.

CASE 27.—A 42-year-old woman had had symptoms of insufficiency for ten to fifteen years. On admission to the hospital, her most obvious symptoms were dyspnea and cyanosis. She had a palpable liver, only slight edema, a venous pressure of 19 cm. H_2O and a heart volume of 1,980 cubic centimeters. The corpuscular weight, determined in this decompensation phase, was found to be 2,240 grams or 43 grams per kilogram of dry body weight. The whole blood measured 4,200 grams and the plasma 1,960 grams. The hematocrit reading, 51 per cent, also suggested an abnormally high proportion of erythrocytes (Table I and Fig. 10).

Fig. 10 shows that equilibrium was established late (not until the fiftieth minute), but that the activity remained constant up to the sixth hour after injection. Without doubt the labelled blood corpuscles were delayed in organs where the circulation was slow and in the dilated heart and did not reach the faster circulation and mix completely with the rest of the blood promptly.

DISCUSSION

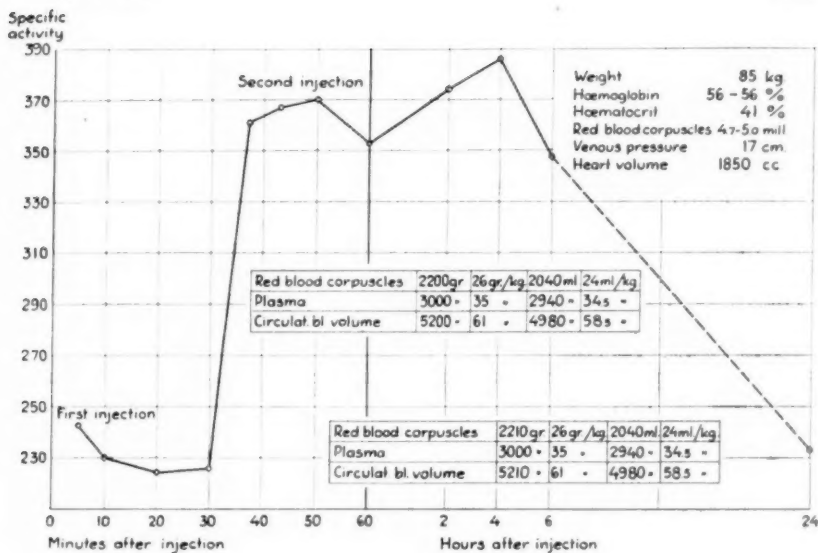
A comparison between the corpuscular weight (in grams per kilogram of dry body weight) in normal patients and in patients with heart disease during compensation and decompensation is shown in the form of a graph in Fig. 11.

Case 26

Heart Failure

April 11, 1946

J. priv.



Case 26

Heart Failure

June 8 1946

J. priv.

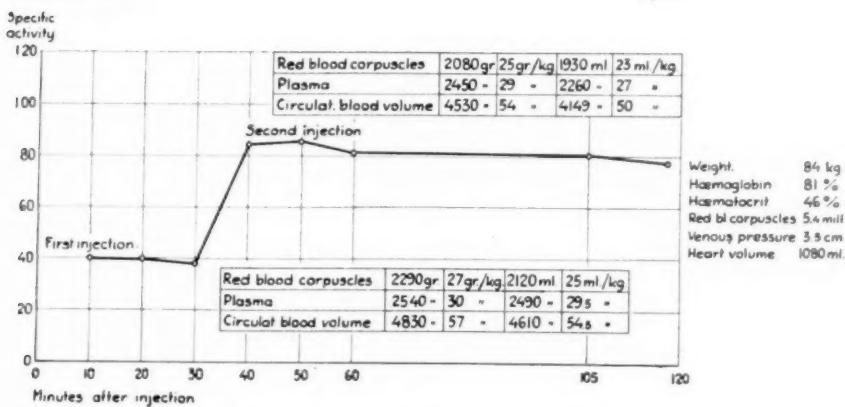


Fig. 9. - Findings in Case 26. See text.

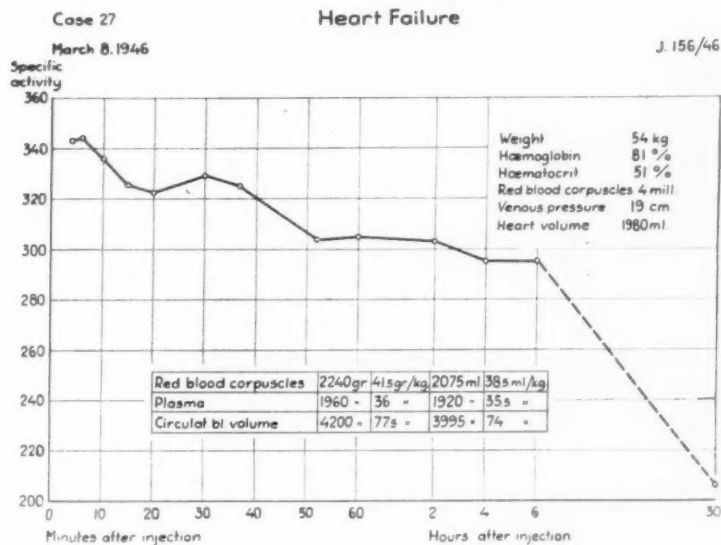


Fig. 10. — Findings in Case 27. See text.

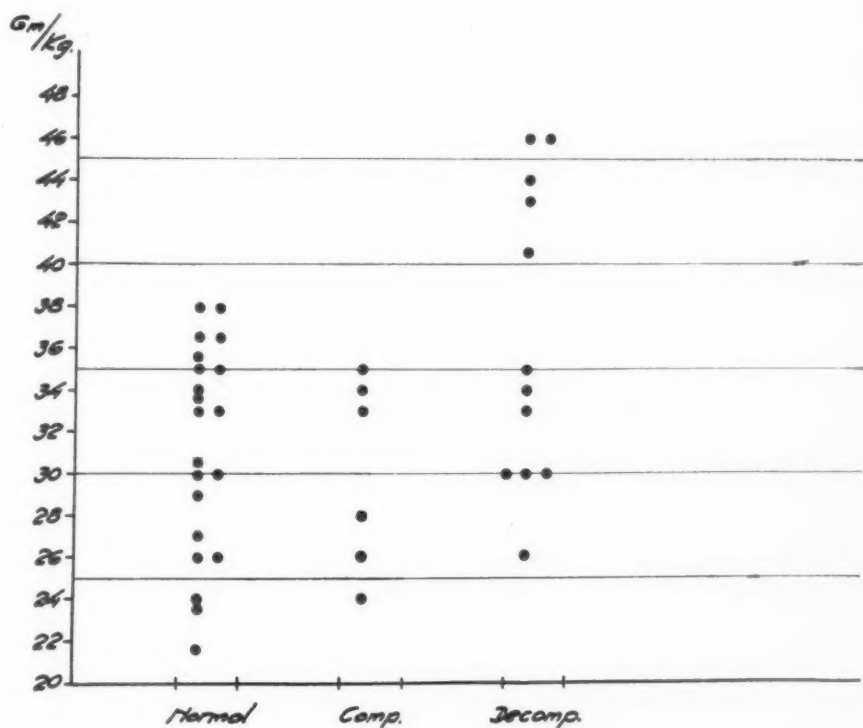


Fig. 11. — Comparison of weight of corpuscles (in grams per kilogram of dry body weight) in normal subjects with the weight of those in patients with heart disease during the stages of decompensation and compensation.

The average corpuscular weight in normal individuals, as previously mentioned, is 31.2 grams $\pm 3 \times 1.06$. The range in these normal cases is from 21.5 to 38 grams. The average weight of the corpuscles in decompensated patients, on the other hand, is 36.4 grams per kilogram $\pm 3 \times 1.94$. The range in this group is from 26 to 46 grams. The increase in corpuscular weight in decompensation is thus statistically demonstrated. The range in the small number of compensated cardiac patients appears to correspond more or less to the normal. It is thus seen that the corpuscular weight per kilogram of dry body weight in patients with cardiac insufficiency falls, after compensation has occurred, to the level observed in normal patients. In some cases, restoration of compensation was not only accompanied by a reduction in the amount of whole blood and plasma, indicating a loss of fluid, but also by a reduction in the total number of erythrocytes. In most cases, decompensation was accompanied by an increase in the amount of whole blood and of erythrocytes. It appears that the increase in whole blood, which is a feature of decompensation, is particularly pronounced in patients with severe edema, whereas, if the decompensation expresses itself mainly in pulmonary congestion, and peripheral edema is insignificant, then there is only a slight increase in the number of red corpuscles. With the material at our disposal, we cannot yet draw any definite conclusions as to a correlation between the duration of insufficiency symptoms and the total number of red blood corpuscles. It is not improbable, however, that a significant increase in the number of erythrocytes actually occurs in patients who have suffered from insufficiency for many years.

It is also clear from the investigation that an abnormally high venous pressure must not be regarded as a sign of excess blood. It is precisely in those cases where pulmonary stasis is the only or the primary sign of decompensation and the venous pressure is abnormally high that one finds the volume of blood to be practically normal. The venous pressure does not, therefore, determine the volume of the blood nor is the latter the sole factor regulating the venous pressure. In cases with both excessive blood volume and high venous pressure, there is a reduction in both during recovery. Meneeley and Kaltreider⁴³ and others have also drawn attention to this absence of correlation between venous pressure and blood volume.

We have already remarked upon certain curious features of the various graphs which show the specific activity of the erythrocytes at different times during decompensation and compensation. Thus, one cannot fail to notice that in decompensation the activity remains constant for a remarkably long time: for four, six, or even twenty-four hours after injection. In certain cases activity actually increases for these long periods of time. After compensation has been restored, the appearance of the graphs undergoes a gradual change; the fall in activity sets in earlier and finally the graph appears more or less normal. Case 21 illustrates these changes very well.

Fig. 12 shows in the form of a graph the fall in the activity of the erythrocytes over a period of twenty-four hours in normal subjects and in decompensated patients. Each plotted point represents the average for a number of measurements. The time values are expressed as percentages of the specific activity of

the equilibrium value. The graphs show that the fall in activity almost corresponds to a straight line and that it commences earlier and proceeds more rapidly in normal cases than in those where decompensation is present. The same is true of the activity of the plasma; Fig. 13 shows in graph form the fall in plasma activity expressed in percentages of the specific activity at the tenth minute. A conceivable explanation of these phenomena is that in cases of cardiac insufficiency the activated blood is retained somewhere in the body, possibly in some congested region such as the portal system and liver, and delayed in reach-

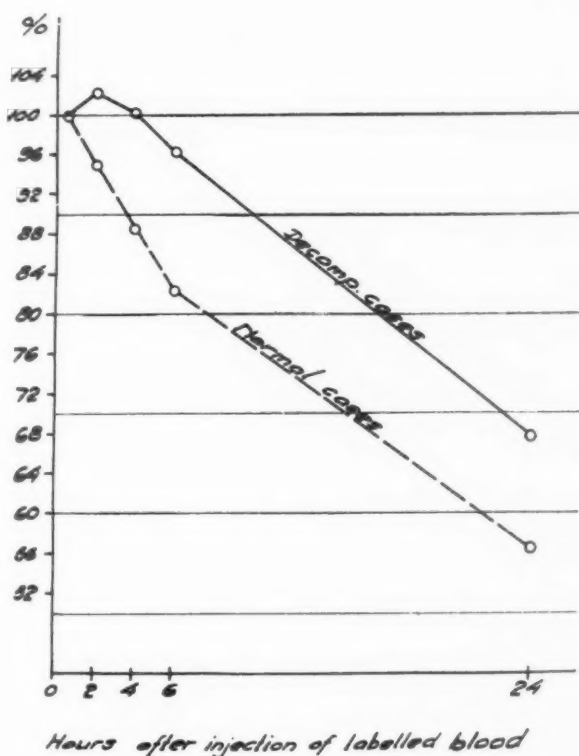


Fig. 12.—The fall in the activity of the erythrocytes during a period of twenty-four hours in normal subjects and in patients with decompensation.

ing the faster circulation from which the venous samples are taken. When compensation occurs, the portal stasis is eliminated, the circulation is accelerated, and the blood corpuscles reach the arm vein sooner. The result is that the decline in activity of blood corpuscles and plasma resembles that seen in normal persons. It is also possible that the permeability of the corpuscular membrane to the phosphate ion P^{32} may be different in the normal and decompensated circulations and that this may affect the activity. Thus, a blood corpuscle with a high resistance in decompensation might less easily give up its phosphate ions once it has been activated.

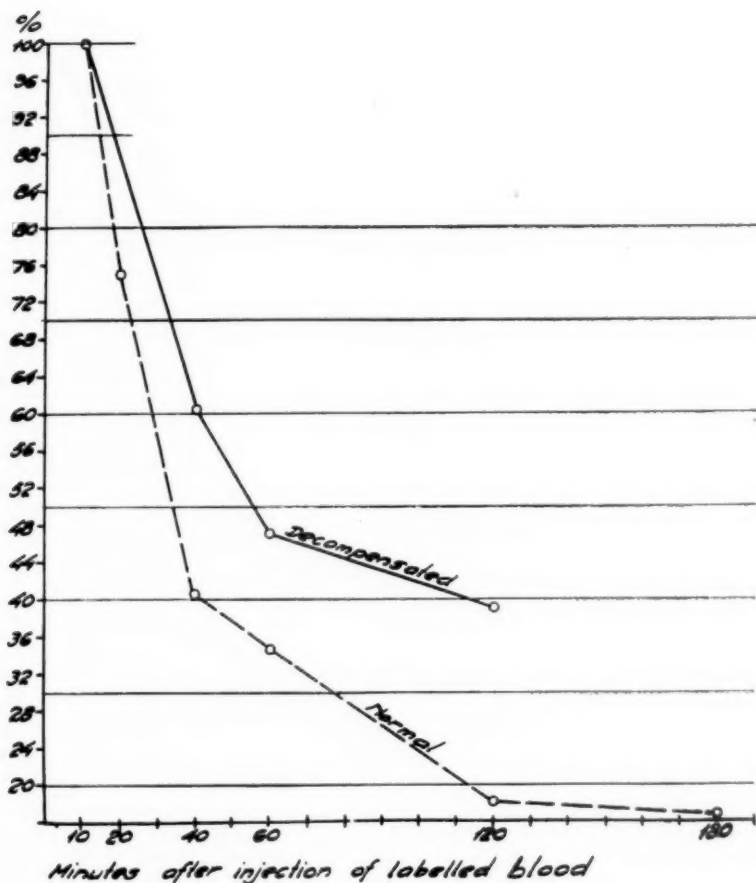


Fig. 13.—The fall in the activity of the plasma during a period of twenty-four hours in normal subjects and in patients with decompensation. The fall in activity is expressed in percentages of the specific activity at the tenth minute after injection.

SUMMARY

1. The different methods of estimating blood volume are reviewed. The inherent faults of the blue azo dye method for estimating plasma volume are stressed. Since the concentration of this substance constantly diminishes in the circulating blood, the point at which equilibrium (balance) is established is difficult to determine accurately. Even in the carbon monoxide method there is no considerable period when there is a constant amount of the test substance in the circulating blood, since a quantity, difficult to measure, is absorbed by the myoglobin. The introduction of Hevesy's method for labelling the blood corpuscles with radioactive phosphorus, however, has contributed greatly to the study of different problems of circulation. One of the advantages of this method lies in the fact that the test substance maintains a constant activity in the blood for as long as an hour. Certain opinions and conclusions that have come from

experience with this method are discussed. The use of the hematocrit for estimating the blood volume is also discussed.

2. A variation of the original method which employs radioactivated whole blood (both corpuscles and plasma) is described. The blood corpuscles maintain their activity up to sixty minutes, while the activity of plasma falls to one-tenth of its original value after five minutes.

3. By the use of this procedure the quantity of blood corpuscles was estimated in seven cardiac patients both in the stage of decompensation and after compensation had been restored. In decompensated cardiac patients there is not only an increase in the total quantity of blood and plasma, but also in the amount of erythrocytes. After compensation is restored, both the plasma and blood corpuscles decrease in quantity. There is a clear difference in the quantity of blood corpuscles, measured in grams per kilogram of dry body weight (the weight of the body when there is no edema), in decompensated patients and in normal subjects. In decompensated patients the quantity of erythrocytes is, on the average, 36.4 grams per kilogram of dry body weight; in normal subjects, this value is 31.2 grams per kilogram of dry body weight. About the same quantity of erythrocytes is found in compensated cardiac patients as is found in normal subjects. In normal subjects there is a correlation between the total quantity of blood corpuscles and the body weight.

4. The importance of a knowledge of the form of the dilution curve for the labelled blood corpuscles is stressed. Estimation of the circulation time by this method in cardiac patients with dilated hearts, but no peripheral edema, supports the view that blood is retained in dilated hearts and that this factor greatly influences the estimation of the circulation time. A comparison between the dilution curves in decompensated patients and normal subjects shows that the activity is reduced slowly in decompensated patients. This seems to indicate that the activated blood is kept for a certain time within the congested area.

We wish to express our sincere thanks to the Swedish Board of Medical Research, the financial assistance of which has enabled us to carry out these investigations.

We present our compliments to Prof. G. de Hevesy, who has constantly shown an interest in our studies. We are likewise grateful to Prof. M. Siegbahn, who procured radioactive phosphorus for our work.

REFERENCES

1. Keith, N. M., Rowntree, L. G., and Geraghty, J. T.: A Method for the Determination of Plasma and Blood, *Arch. Int. Med.* **16**:547, 1915.
2. Dawson, A. B., Evans, H. M., and Whipple, G. H.: Blood Volume Studies; Behavior of Large Series of Dyes Introduced Into Circulating Blood, *Am. J. Physiol.* **51**:232, 1920.
3. (a) Gibson, J. G., Jr., and Evans, W. A., Jr.: Clinical Studies of Blood Volume; Clinical Application of Method Employing Azo Dye "Evans Blue" and Spectrophotometer, *J. Clin. Investigation* **16**:301, 1937.
- (b) Gibson, J. G., Jr., and Evans, W. A., Jr.: Clinical Studies of Blood Volume; Relation of Plasma and Total Blood Volume to Venous Pressure, Blood Velocity Rate, Physical Measurements, Age, and Sex in 90 Normal Humans, *J. Clin. Investigation* **16**:317, 1937.
- (c) Gibson, J. G., Jr., and Evans, W. A., Jr.: Clinical Studies of Blood Volume; Changes in Blood Volume, Venous Pressure, and Blood Velocity Rate in Chronic Congestive Heart Failure, *J. Clin. Investigation* **16**:851, 1937.

4. (a) Gregersen, M.: Practical Method for Determination of Blood Volume With Dye T-1824; Survey of Present Basis of Dye Method and Its Clinical Applications, *J. Lab. & Clin. Med.* **29**:1266, 1944.
- (b) Gregersen, M. I., Gibson, J. J., and Stead, E. A.: Plasma Volume Determination With Dyes; Errors in Colorimetry; Use of the Blue Dye T-1824, *Am. J. Physiol.* **113**:54, 1935.
5. Cardozo, E. L.: The Disappearance of the Blue Dye T-1824 From the Blood Stream Into the Thoracic Duct Lymph, *Arch. néerl. de physiol.* **25**:410, 1940.
6. King, B. G., Cole, K. S., and Oppenheimer, E. T.: Disappearance Curves of T-1824 After Its Injection Into Blood Stream, *Am. J. Physiol.* **138**:636, 1943.
7. Gregersen, M. I., and Rawson, R. A.: Disappearance of T-1824 and Structurally Related Dyes From Blood Stream, *Am. J. Physiol.* **138**:698, 1943.
8. Gréhant, N., and Quinquaud, E.: *Journ. de l'anat. et physiol.* **43**:303, 1888.
9. Salvesen, H. A.: Determination Carbon Monoxide in Blood, *J. Biol. Chem.* **40**:103, 1919.
10. Haldane, J., and Smith, J. L.: The Mass and Oxygen Capacity of the Blood in Man, *J. Physiol.* **25**:331, 1900.
11. Van Slyke, D. D., and Rabscheit-Robbins, F. A.: Gasometric Determination of Small Amounts of Carbon Monoxide in Blood, and Its Application to Blood Volume Studies, *J. Biol. Chem.* **72**:39, 1927.
12. Arnold, H. R., Carrier, E. B., Smith, H. P., and Whipple, G. H.: Blood Volume Studies; Carbon Monoxide—Its Accuracy and Limitations, *Am. J. Physiol.* **56**:313, 1921.
13. McIntosh, R.: Determination of Circulating Blood Volume in Infants by Carbon Monoxide Method, *J. Clin. Investigation* **7**:203, 1929.
14. Steinmann, B.: Ueber das Verhalten des zirkulierenden Blutes beim Herzkranken, *Arch. f. exper. Path. u. Pharmacol.* **193**:24, 1939.
15. Steinmann, B.: Ueber die Bestimmung der zirkulierenden Blutmenge beim Menschen, *Arch. f. exper. Path. u. Pharmacol.* **191**:237, 1938.
15. Plesch, J.: Physiology and Pathology of Amount of Blood, *Ztschr. f. klin. Med.* **93**:241, 1922.
17. Grosse-Brockhoff, F., and Molineus, W.: Untersuchungen über die Blutdepots des Menschen, *Deutsches Arch. f. klin. Med.* **185**:481, 1940.
18. Chang, H. C., and Harrop, G. A., Jr.: Determination of Circulating Blood Volume With Carbon Monoxide, *J. Clin. Investigation* **5**:393, 1928.
19. Hartmann, H.: Ueber die Grundlagen der Differenzphotometrie und ihre Anwendung zur Bestimmung geringer Kohlenoxydmengen im Blut, *Ergebn. d. Physiol.* **39**:413, 1937.
20. Smith, H. P., Arnold, H. R., and Whipple, G. H.: Blood Volume Studies; Comparative Values of Welcker, Carbon Monoxide and Dye Methods for Blood Volume Determinations; Accurate Estimation of Absolute Blood Volume, *Am. J. Physiol.* **56**:336, 1921.
21. Stead, E. A., Jr., and Ebert, R. V.: Relationship of Plasma Volume and Cell Plasma Ratio to Total Red Cell Volume, *Am. J. Physiol.* **132**:411, 1941.
22. Hahn, P. F., Ross, J. R., Bale, W. F., Balfour, W. M., and Whipple, G. H.: Red Cell and Plasma Volumes (Circulating and Total) as Determined by Radio Iron and by Dye, *J. Exper. Med.* **75**:221, 1942.
23. Fahraeus, R.: Suspension Stability of Blood, *Physiol. Rev.* **9**:241, 1929.
24. Bazett, H. C., Sunderman, F. W., Maxfield, M. E., and Scott, J. C.: Comparison of Estimates of Blood Volume Made by Congo Red and by Carbon Monoxide, *Am. J. Physiol.* **129**:309, 1940.
25. Hahn, P. F., Bale, W. F., and Balfour, W. M.: Radioactive Iron Used to Study Red Blood Cells Over Long Periods; Constancy of Total Blood Volume in Dog, *Am. J. Physiol.* **135**:600, 1942.
26. Hahn, L., and Hevesy, G.: A Method of Blood Volume Determination, *Acta physiol. Scandinav.* **1**:3, 1940.
27. Hahn, L., and Hevesy, G.: Rate of Penetration of Ions Into Erythrocytes, *Acta physiol. Scandinav.* **3**:193, 1942.
28. Hevesy, G., and Zerahn, K.: Determination of the Blood Corpuscle Content, *Acta physiol. Scandinav.* **4**:376, 1942.
29. Nylin, G., and Malm, M.: Concentration of Red Blood Corpuscles Containing Labeled Phosphorous Compounds in Arterial Blood After Intravenous Injection; Preliminary Report, *Am. J. M. Sc.* **207**:743, 1944.

30. Nylin, G.: Dilution Curve of Activity in Arterial Blood After Intravenous Injection of Labeled Corpuscles, *AM. HEART J.* **30**:1, 1945.
31. Nylin, G.: Blood Volume Determinations With Radioactive Phosphorus, *Brit. Heart J.* **7**:81, 1945.
32. Nylin, G.: *K. Svenska Vetenskapsakademien, Arkiv för Kemi, Mineralogi och Geologi* **20**:17, 1945.
33. Nylin, G., and Malmstrom, G.: Further Investigation Concerning the Interpretation of Prolonged Circulation Time in Cardiology, *Cardiologia* **5**:333, 1941.
34. Gernandt, B., and Nylin, G.: The Relation Between Circulation Time and the Amount of the Residual Blood of the Heart, *AM. HEART J.* **32**:411, 1946.
35. Hevesy, G., Køster, K. H., Sørensen, G., Warburg, E., and Zerahn, K.: Red Corpuscle Content of Circulating Blood Determined by Labeled Erythrocytes With Radiophosphorous, *Acta med. Scandinav.* **116**:561, 1944.
36. Brown, F. A., Jr., Hempelmann, L. H., Jr., and Elman, R.: Determination of Blood Volume With Red Blood Cells Containing Radioactive Phosphorous (P^{32}), *Science* **96**:323, 1942.
37. Chapin, M. A., and Ross, J. F.: Determination of True Cell Volume by Dye Dilution, by Protein Dilution, and With Radioactive Iron. Error of Centrifuge Hematocrit, *Am. J. Physiol.* **137**:447, 1942.
38. Hahn, P. F., and Bale, W. F.: Linear Relationship Between Circulating Red Cell Mass and Venous Hematocrit as Determined With Radioactive Iron, *Am. J. Physiol.* **136**:314, 1942.
39. Wollheim, E.: Die zirkulierende Blutmenge und ihre Bedeutung für Kompensation und Dekompensation des Kreislaufs, *Ztschr. f. klin. Med.* **116**:269, 1931.
40. Ewig, W., and Hinsberg, K.: Kreislaufstudien, *Ztschr. f. klin. Med.* **115**:693, 1931.
41. Schürmeyer, A.: Ueber Blutmengenbestimmungen bei Herzfehlern, *Verhandl. d. deutsch. Gesellsch. f. inn. Med.* **40**:388, 1928.
42. Seymour, W. B., Pritchard, W. H., and Longley, L. P.: Cardiac Output, Blood and Interstitial Fluid Volumes, Total Circulating Serum Protein, and Kidney Function During Cardiac Failure and After Improvement, *J. Clin. Investigation* **21**:229, 1942.
43. Meneely, G. R., and Kaltreider, N. L.: Study of Volume of Blood in Congestive Heart Failure. Relation to Other Measurements in 15 Patients, *J. Clin. Investigation* **22**:521, 1943.
44. Waller, J. V., Blumgart, H. L., and Volk, M. C.: Studies of Blood in Congestive Heart Failure, With Particular Reference to Reticulocytes, Erythrocyte Fragility, Bili-rubinemia, Urobilinogen Excretion and Changes in Blood Volume, *Arch. Int. Med.* **66**:1230, 1940.
45. Ehrström, M. C.: Blutstoffwechsel und Urolilinurie bei Herz-insuffizienz, *Acta med. Scandinav.* **88**:517, 1936.
46. Anderson, R. S.: Use of Radioactive Phosphorus for Determining Circulating Erythrocyte Volumes, *Am. J. Physiol.* **137**:539, 1942.
47. Asmussen, E.: On Determination of Blood Volume by CO-method, *Acta physiol. Scandinav.* **3**:156, 1942.
48. Hedin, S. G.: Der hämotokrit, ein neuer Apparat zur Untersuchung des Blutes, *Skandinav. Arch. f. Physiol.* **2**:134, 1891.
49. Ponder, E.: Hematocrit Method, *M. Physics*, p. 597, 1944.
50. Miller, W. G.: Observations on the Haematocrite Method of Measuring the Volume of Erythrocytes, *Quart. J. Exper. Physiol.* **15**:187, 1925.
51. Moritz, F., and Tabora, D.: Ueber eine Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, *Deutsches. Arch. f. klin. Med.* **98**:475, 1910.

ELECTROCARDIOGRAMS WITH LARGE, UPRIGHT T WAVES AND LONG Q-T INTERVALS

EDWIN BYER, M.D., RICHARD ASHMAN, PH.D., AND LOUIS A. TOTH, PH.D.
NEW ORLEANS, LA.

ELECTROCARDIOGRAMS with rather large, upright T waves are not very unusual. Among adults, they are most often seen in sinus bradycardia, and usually in association with R waves of average or greater than average amplitude. In healthy persons whose electrocardiograms are of this type it has been suggested that the spatial ventricular gradient is parallel to the frontal plane, and the magnitude of the gradient is large because of the bradycardia.¹

In a later statistical study, the mean magnitude of the ventricular gradient* of eighty men was estimated at 11.77 ± 0.39 units of 4 microvolt-seconds each, each unit being equal to a single small rectangle on the film with usual standardization and timing.² The standard deviation was 4.52 ± 0.24 units. Hence, the normal range in magnitude of the gradient appeared to be from -1.8 to $+25.3$ units. This indicates that about one normal person in 370 will have a gradient outside this range. In a group of eighty-four women, G (the magnitude of the gradient) averaged 11.34 ± 0.27 units, the standard deviation was 3.67 ± 0.19 units, and the range at 3 standard deviations was $+0.3$ to $+22.3$ units of area. These figures have the value that they enable us to say that in certain cases the gradient and the T waves are unusually or abnormally large.

The electrocardiogram shown in Fig. 1 was taken on April 8, 1938, on a 47-year-old ambulatory Negro woman who complained of substernal "heaviness," occasional sharp pains over the precordium, and palpitation on exertion. At that time arterial blood pressure was 270/158 and the Wassermann was negative.

No record is available for the period between April, 1938, and December, 1939. At this later date on the occasion of a visit to a friend's house the patient was seized with a "smothering" feeling and ascending numbness of the left lower extremity. She attempted to walk home, but the symptoms became more severe and the smothering feeling changed to severe substernal pain with radiation down the left arm. This was shortly followed by a period of unconsciousness during which time she had several convulsions and vomited. Consciousness returned spontaneously in a few minutes. On his arrival, an ambulance physician noted cyanosis and profuse sweating. A small white pill placed under the patient's tongue brought relief from the substernal pain. She was placed at bed rest.

On Jan. 2, 1940, a physician was consulted for the precordial pain, and at this time the patient was hospitalized. Physical examination revealed an arterial blood pressure of 242/160, a heart

From the Department of Physiology, Louisiana State University School of Medicine, and The Charity Hospital of Louisiana.

Received for publication Aug. 26, 1946.

* The ventricular gradient of Wilson is the manifest mean area of the whole ventricular complex, QRS-T.

rate of 75 beats per minute with a regular rhythm, and marked cardiac enlargement. The aortic second sound was accentuated. Neurological examination was reported as showing no abnormalities. The diagnosis was recorded as "hypertensive cardiovascular disease, coronary occlusion versus angina pectoris, and possible hypertensive encephalopathy." She left the hospital in about three weeks.

On Dec. 2, 1940, the patient was again admitted to the hospital following a "falling out" attack at home. She was conscious but semistuporous on admission and complained of severe right frontal headache. On physical examination the arterial blood pressure was 235/130. The only neurological finding was weakness of the left hand. A spinal tap revealed a spinal fluid pressure of 300 mm. of water and a grossly bloody fluid with a clear supernatant portion on centrifugation.

On December 3, the patient had meningismus with positive Brudzinski and Kernig signs. Left hemiparesis was present.

On December 4, the electrocardiogram shown in Fig. 2 was taken. The blood urea nitrogen on this date was 78/4 mg. per cent.

On December 6, the spinal fluid was xanthochromic and under pressure of 150 mm. of water. By December 9, the urea nitrogen was 14 mg. per cent and the patient's neurological signs were diminishing.

On Aug. 8, 1943, the patient was sent in from the clinic for another electrocardiogram with the complaint of "pain over her heart, smothering spells, and weakness." Arterial blood pressure at this time was 180/105. At no time throughout this period had she received digitalis, nor were there signs of congestive failure.

Electrocardiographic Findings.—The electrocardiogram of Fig. 1, taken in 1938, is not unusual. The mean heart rate is 63 per minute, the P-R interval is 0.145 to 0.165 second, the duration of the QRS complex is 0.09 second or

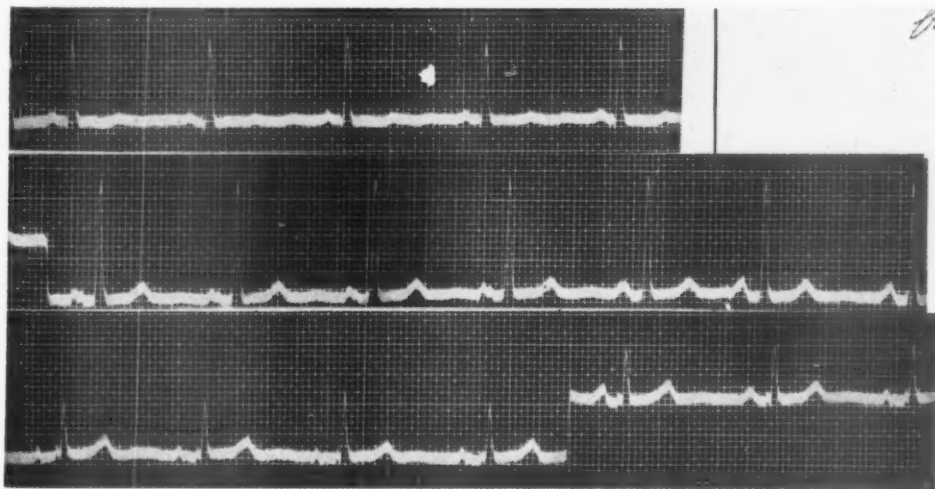


Fig. 1.—Electrocardiogram taken April 8, 1938. The low T wave in Lead I is partly primary and partly secondary.¹¹ On Jan. 20, 1940, another electrocardiogram was like this one, except for lower T waves in all limb leads; the heart rate was practically the same.

slightly more, and the Q-T interval is 0.41 second, which puts it near the upper limit of the normal. The magnitude of A_{QRS} is 14.0 units (56.0 microvolt-seconds) and, therefore, large,¹ suggesting hypertrophy of the left ventricle. The T wave is low in Lead I and upright in Lead III; in the presence of this QRS pattern,

this is abnormal. There is a shift of pacemaker shown by the change in form of the P waves. No precordial leads were taken.

On Jan. 20, 1940, another electrocardiogram was taken. It revealed only minor changes from Fig. 1, mainly a decrease in height of T_2 and T_3 . The Q-T interval was unchanged. The precordial lead (CF4) was like that of Fig. 2, the T waves being upright.

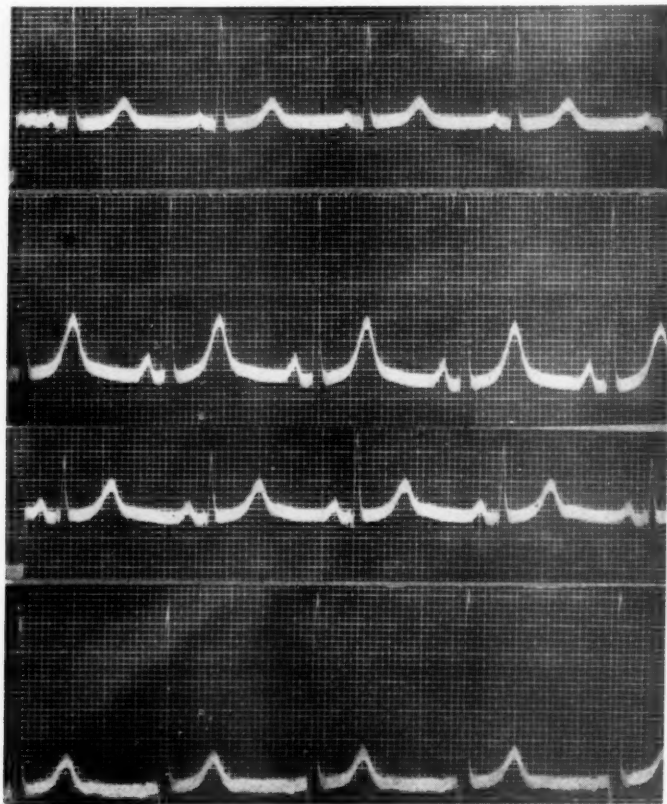


Fig. 2.—Electrocardiogram taken two days after admission to hospital in a semistuporous state in December, 1940.

The electrocardiogram of Fig. 2 was taken on Dec. 4, 1940, two days after the cerebrovascular accident. The rate is still about 63 per minute. The P-R interval is 0.16 second; the QRS duration is about 0.10 second; the Q-T interval, measured in Lead I, is fully 0.49 second. In Leads II and III, the end of the T wave is indefinite and blends with the U waves. R_1 and R_2 are larger than before. A_{QRS} is now nearly 17.0 units. The T waves are large and wide. The ventricular gradient is little changed in direction since 1938, but its magnitude has gone up from not quite 19.0 units to nearly 43.0 units.

On Dec. 13, 1940, the electrocardiogram of Fig. 3 was taken. The QRS complexes are essentially unchanged, but the large T waves have disappeared,

and the T waves are all low. The Q-T interval is again 0.40 second, the heart rate now being 75 per minute. As in Fig. 2, the P waves are higher than in Fig. 1; but the shift in pacemaker in Fig. 1 suggests that such a shift is the main reason for this increase.

The limb leads of the electrocardiogram of Aug. 8, 1943, were very similar to Fig. 1; but the R waves were larger, as in Fig. 3, and the Q-T interval in CF₄ was 0.45 second, the T wave being slightly deeper than in Fig. 3. The heart rate was 65 per minute.

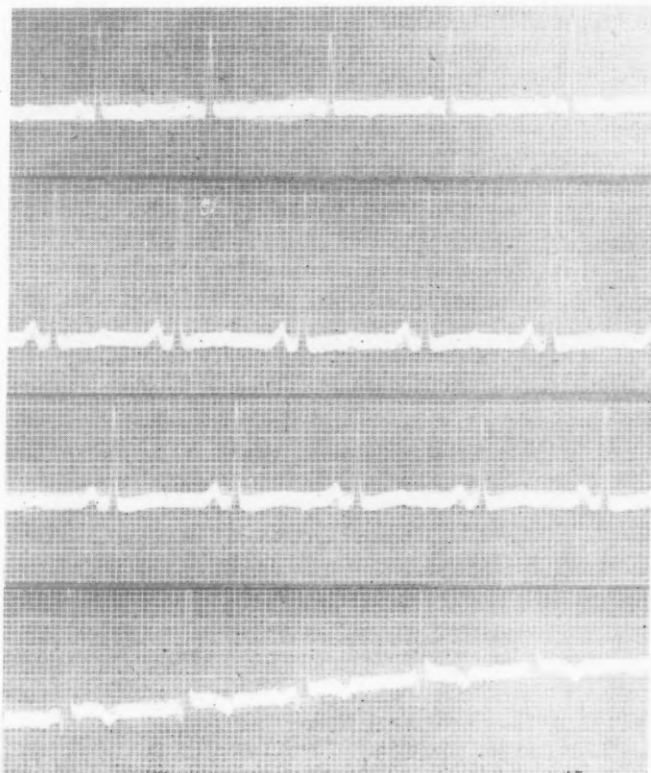


Fig. 3.—Electrocardiogram of Dec. 13, 1940, nine days after that of Fig. 2.

The striking change in this series of electrocardiograms is the increase in the height of the T waves which was recorded on the second day after the cerebrovascular accident, and the prolongation of the Q-T interval from a duration near the upper limit of the normal to 0.49 second, which is 0.08 above the upper limit.³ These changes had disappeared nine days later.

Just how large the gradient is in Fig. 3 is best demonstrated by statistical methods. If we take the average G for women to be 11.34 units, as stated in the introduction, the G in this case exceeds the average by over 31 units. If we take 4.0 units as the standard deviation, then the gradient in this case exceeds the

average by nearly 8 standard deviations. This is very far outside the normal range of gradient magnitude.

Without searching our complete files, we have found the electrocardiograms from five other cases in which large, upright T waves appeared; in two of the patients cerebrovascular accidents had occurred, while one patient had severe hypertensive encephalopathy. The changes in these patients were not so extreme as in the case described in detail.

The first of these five patients was a Negro woman, 47 years of age, whose arterial pressure was 218/148, and who had a "falling out spell," with loss of consciousness for several hours, on March 2, 1941. The first electrocardiogram, taken on March 7, indicated left ventricular hypertrophy. The T waves were low, T_1 being slightly inverted. A sharply inverted T wave in the precordial lead (CF_4) suggested ischemia of the subjacent heart wall. This patient subsequently had severe attacks of vertigo, headaches, and weakness, but there is no record of abnormal neurological findings. A second electrocardiogram, taken on August 15 of the same year, was unchanged except that T_1 , T_2 , and T_4 were rather high, and the Q-T interval was moderately prolonged. On July 27, 1942, the patient had a cerebrovascular accident with sudden loss of consciousness, followed by rapid onset of acute pulmonary edema. The arterial pressure was 223/185 at this time. The patient died within a few hours. No electrocardiogram was obtained.

The second patient was a Negro woman, 28 years old. She was admitted to the hospital on May 4, 1943, with aphasia, and was one month post partum. The pregnancy and delivery had apparently been normal. On admission the arterial pressure was 148/100. The rest of the physical examination was not contributory. Her arterial pressure in 1941 and 1945 was consistently well within the normal range. The electrocardiogram, taken on May 4, 1943, is shown in Fig. 4. The QRS complexes are within the normal range. The Q-T interval is prolonged moderately. Her gradient, at 24.4 units, is not absolutely very large, but it is large at a heart rate of 80 to 85 per minute (in Leads I and III) and with an A_{QRS} of 4.6 units. It lies at nearly 4 standard deviations from the mean.

The third patient was also a Negro woman, 49 years of age. Arterial blood pressure on admission to the hospital was 180/80. A cerebrovascular accident occurred at 6:30 P. M., Aug. 14, 1946, and the first electrocardiogram was taken on Aug. 16, 1946. The gradient was not absolutely large, because of a slight depression of the RS-T segments in Leads I and II. The diagnosis was "cerebral hemorrhage with left hemiplegia." The spinal fluid was grossly bloody, and the pressure was 200 mm. of water.

A fourth patient was a 29-year-old white woman, who, on July 1, 1941, had a normal electrocardiogram, and arterial hypertension. The electrocardiogram at that time was within normal limits, and the T waves were not high. Two months later, the blood pressure was 240/150, and the T waves in Leads I and II were large. Two years later, when the arterial pressure was reported to be 260/170, T_1 had become isoelectric (a primary change) and T_3 high. The QRS changes suggested hypertrophy of the left ventricle. Shortly afterward the patient died. The final diagnosis was "malignant hypertension."

The fifth patient was a 59-year-old white woman, whose blood pressure was 210/110. No other relevant findings are available.

Finally, we have found one apparently normal electrocardiogram from a 32-year-old Negro man. The clinical diagnosis was syphilitic aortitis. His complaints were dyspnea, substernal pain, and "weak spells." The arterial pressure was 116/78 to 110/70. The electrocardiogram shows normal QRS complexes, T waves of quite normal appearance, though rather high and wide, and a Q-T interval which is just over the upper "normal" limit. The gradient is 29.5 units, and lies at 3.9 standard deviations from the mean. An earlier electrocardiogram on this patient had the same G, but the P-R interval varied from 0.22 to 0.26 second. Statistically, the G of one normal person in several thousand may reach this magnitude. This is the largest G we have observed in an apparently quite normal electrocardiogram; but heart disease was probably present. The standardization was correct. We have, however, encountered one larger G from a presumably

normal heart recorded in the first edition of Graybiel and White's Atlas⁴ (p. 33). This is a Wolfe-Parkinson-White syndrome. The gradient is, very approximately, 45.0 units, if the standardization, which is not shown, is correct. This patient had received quinidine, to stop a paroxysmal tachycardia which had persisted for two days. One is reminded of the large, abnormal, T waves sometimes observed after the cessation of a persistent paroxysmal tachycardia,¹² but here the T waves are upright in all leads. If there is myocardial "change," what is its localization?

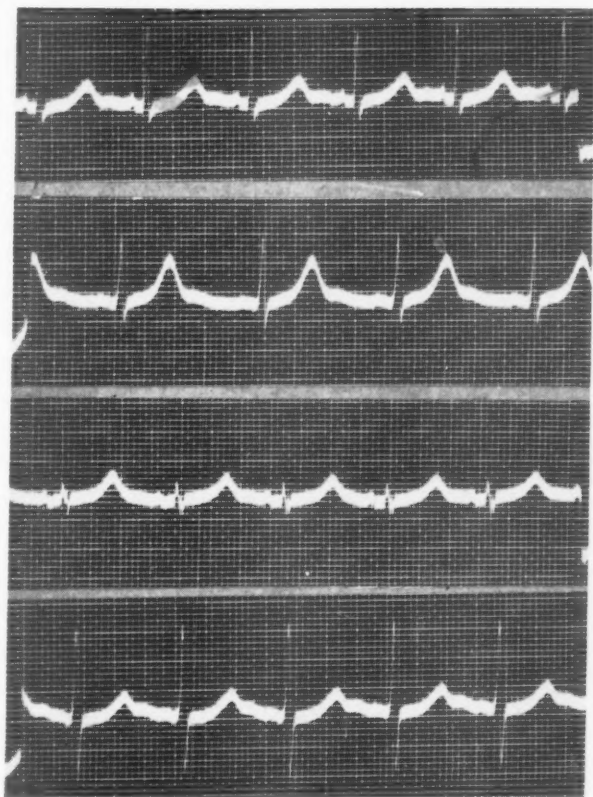


Fig. 4.—Colored woman aged 28 years. This case is described in the text. It may be noted that the ventricular gradient is deviated abnormally to the right.²

We have also seen one or two electrocardiograms with very high, but narrow T waves, which do not seem to belong in the category we are considering in this paper. Furthermore, examples from children's electrocardiograms are not included. Since the child's A_{QRS} is smaller than the adult's, although the mean G is the same,² the child's T wave is larger than the adult's, on the average.

DISCUSSION

In a case which was recently reported by Bayley, the RS-T segments of the electrocardiogram were depressed markedly, especially in Leads I and II.⁵ The depressions were larger than those which may often be ascribed to physiologic factors and were rather clearly indicative of injury. At autopsy it was found that damage of the subendocardial muscle laminae in the left ventricle was greater

than the damage of the subepicardial muscle layers. This paper gave the first direct evidence in man for a suspicion many students of electrocardiography have long entertained, namely, that preponderant subendocardial injury should depress the RS-T segments in two, or in all three, of the limb leads, depending upon heart position. Right ventricular injury may sometimes also do this, but in many cases there is no good evidence implicating that ventricle. In these negative or downward injury displacements we, therefore, see the converse of active pericarditis, which, as a rule, produces elevation of the RS-T segments in at least two limb leads.

In a long series of experiments on the dog, Wolferth, Bellet, Livezey, and Murphy⁶ studied the effect of various procedures upon the RS-T segment with direct leading from the epicardial surface. Among other observations, they found that injection of a potassium chloride solution deep into the left ventricular wall, i.e., to the endocardial surface, produced a negative RS-T segment potential change at the overlying epicardial surface, but injection just beneath the epicardial surface produced an elevation. They also found that extensive trauma of the endocardial surface produced a negative RS-T segment displacement at the epicardial surface. Similar studies, but with indirect leading, have given no consistent results,⁷ although Boyd and Scherf⁸ picture very slight RS-T segment depressions in the limb leads, and state that no elevations occurred when the endocardium was injured.

Bayley⁹ has given a definition of myocardial injury and of ischemia. In the *ischemic stage*, the intensity of polarization of the cell membranes is little, if at all, reduced, but repolarization during inscription of the T wave is slower than it normally is. Not all T waves of the so-called ischemic type, of course, are due to limitation in blood and oxygen supply; but it is very probable that the change in the fiber goes along with a similar, slow, chemical recovery in all cases. In the *injury stage*, the intensity of polarization of the cell membranes is reduced, and most injury displacements, as observed in the human electrocardiogram, are due to this. As Bayley and LaDue¹⁰ point out, both ischemic and injury changes are ante-mortem cellular changes, which disappear when circulation is restored. The electrocardiograms of many patients with coronary arterial disease or arterial hypertension reveal changes of the ischemic type, although there are no changes in the QRS complexes which suggest infarction. As a rule, the ischemic area appears to involve the epicardial (and probably the intramural) fibers more than the endocardial ones.⁹ If, then, the posterior wall is mainly involved, the T wave is inverted in Lead III and, usually, in Lead II. If the anterolateral wall is mainly involved, the T wave is inverted in Lead I, and sometimes in Lead II. The localizations are not in serious dispute, but it is by no means agreed that the endocardial surface is relatively less affected than the more superficial muscle layers.

High T waves in two or three of the limb leads, together with prolonged Q-T intervals, obviously suggest that in these rather rare cases we may be dealing with ischemia preponderantly affecting the inner surface of the left ventricle. None of the cases we report have come to autopsy, and, in view of the

minor nature of the pathologic change at the ischemic stage, as defined by Bayley, it is by no means certain that the microscope would reveal any difference between the different muscle layers in such cases.

Effects of Changing the Temperature of the Dog's Endocardium.—Experiments in which the temperature of the endocardium of the dog's ventricle was changed are reported at greater length elsewhere.¹³ The procedure was to introduce a stiff catheter into the dog's left ventricle by way of the left common carotid artery and aortic valve. At the moment the heart was arrested by faradization of the right vagus nerve, injection of 50 c.c. of Ringer's solution, at different temperatures in different experiments, was begun. Stimulation of the vagus was continued until all of the solution was injected. The purpose of arresting the heart was to permit the solution to come into contact with the endocardial surface of the ventricle and change its temperature before being pumped out. On other occasions the vagus was stimulated for the same length of time, and either no solution or solution at body temperature was injected. Either a limb lead electrocardiogram, or a precordial lead corresponding to the human CF₄, was recorded with each test or control. At the end of the series of experiments on each dog, the thorax was opened and the tip of the catheter was shown to be in the left ventricular chamber.

It is well known that cooling a muscle slows, and warming accelerates, its repolarization. Thus cooling the endocardium should have the same effect as preponderant ischemia of the endocardial muscle layer.

The results of two experiments are illustrated in Figs. 5 and 6, and the temperatures at which the solution entered the syringe are given in the legend. It will be observed that in this dog the period of cardiac arrest alone produced no appreciable change in the height of the T wave in Lead II. In the chest lead, arrest was followed by a slight increase. The cold solution brought about a very large increase in the height of the T wave in both Lead II and CF₄ together with a large increase in the duration of the Q-T interval (Fig. 5). Warming had a smaller effect; yet it not only prevented the increase in the T-wave height due to the slowing in the precordial lead, but brought about a reduction in the amplitude (Fig. 6). In other experiments on another dog, the effect was greater, the T wave being definitely inverted by the warm solution, and the injection of Ringer's solution at 39°C. produced no appreciable change in the T wave. Rather consistently, the first beat after the release or escape from vagus stimulation, both with cooling and warming, showed less T-wave change than the second. The meaning of this is uncertain.

The results of cooling or warming the endocardium demonstrate that changes in the electrical state of that surface of the ventricle affect the form and amplitude of the T wave. They do not, of course, prove that the high and wide T waves in the human cases which we have reported in this paper are due to ischemic changes predominantly affecting the endocardial muscle layer of the left ventricle. They do, however, show that if such an endocardial change were to occur, it should be expected to increase the height and width of the T wave.

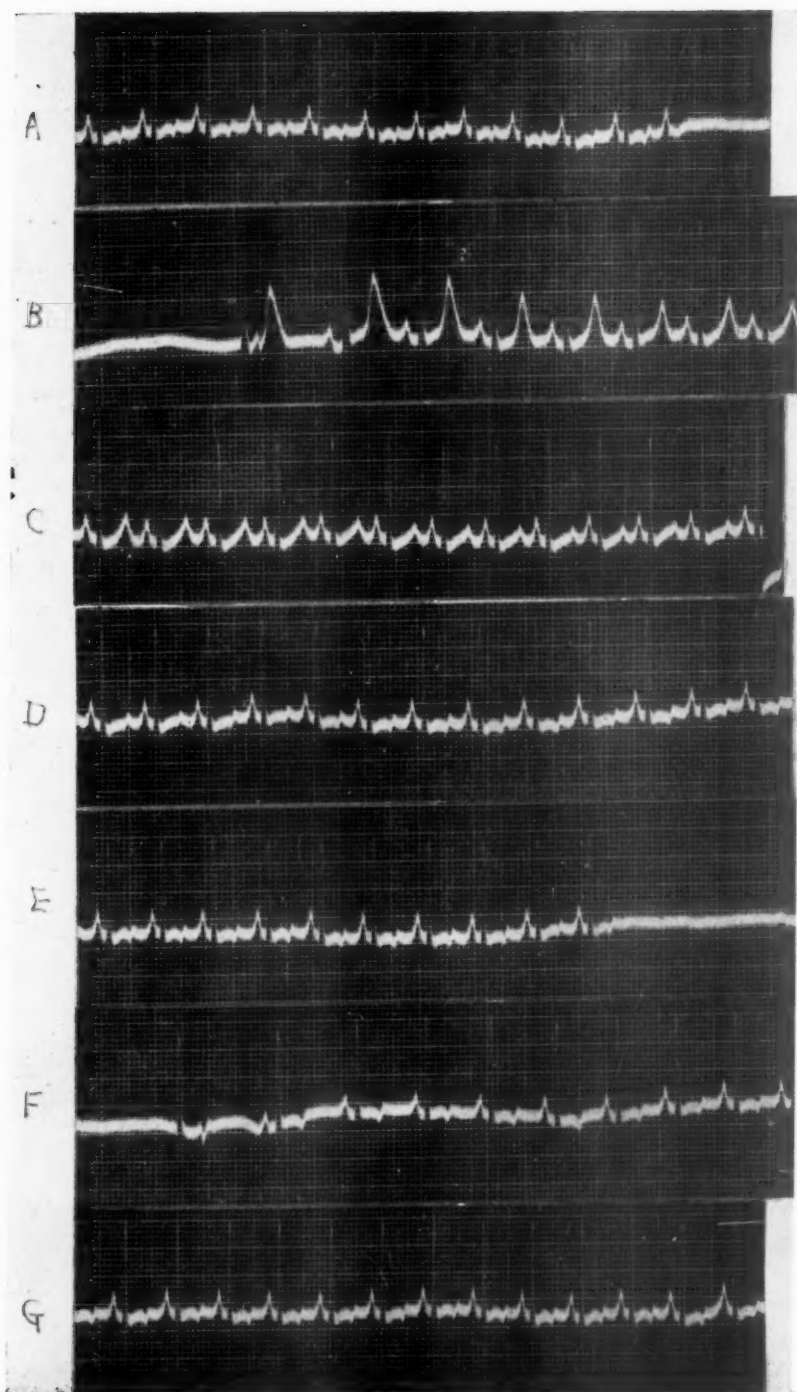


Fig. 5.—Effect of cooling endocardium of left ventricle. All Lead II. Same dog as Fig. 6.
At the end of Strip A, faradization of the right vagus was begun, together with injection into the left ventricular chamber of 50 c.c. of Ringer's solution, which entered the syringe at about 2°C.

Between A and B, four seconds of complete cardiac standstill are omitted. In B, injection completed and vagus stimulation stopped. There is a great increase in the height of the T waves, in spite of increased R waves. The Q-T interval is increased from 0.25 to 0.40 seconds. C and D are continuous with B.

In E, a few minutes after D, vagus stimulation begun, but no injection. Between E and F, four seconds of complete quiescence omitted. In F, stimulation stopped. The changes in the T waves are slight. (In other experiments, not with this dog, injection of Ringer's at body temperature produced no appreciable change). G is continuous with F.

The results of other control vagus stimulations in Lead II were practically identical with this one.

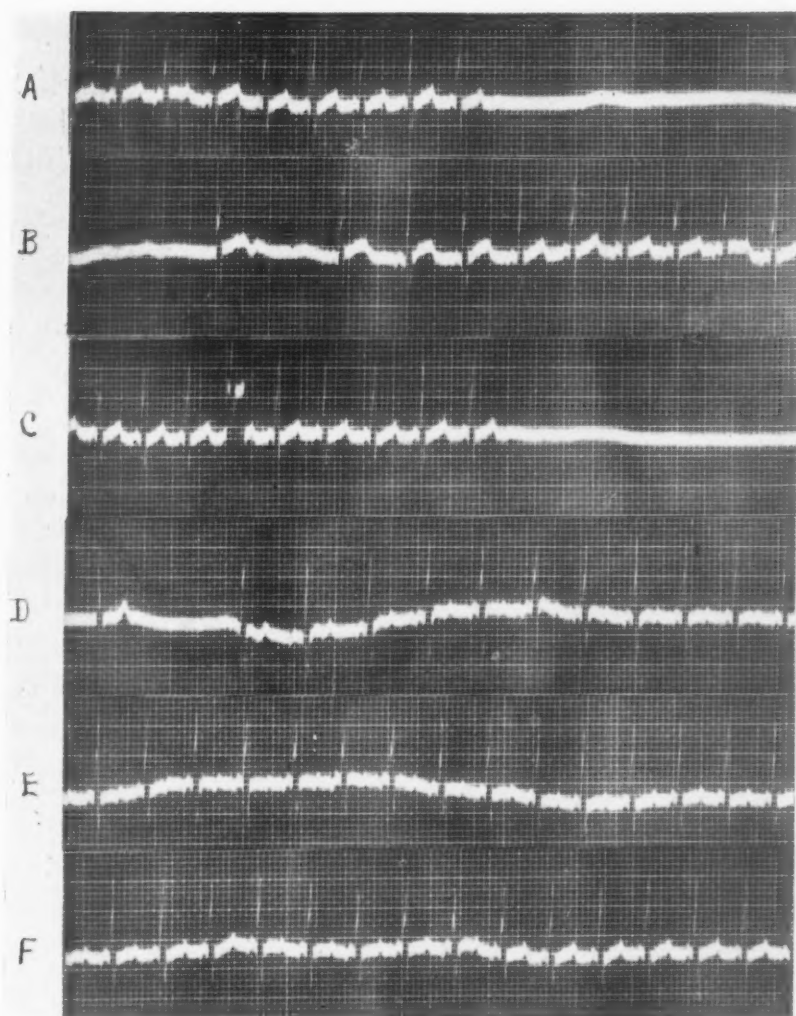


Fig. 6.—Precordial lead from a dog, approximately CF₄.

A shows the beginning of faradization of the right vagus nerve. Between A and B, just two seconds with no heart beats, are omitted. Vagus stimulation stopped early in B. No solution injected. Observe moderate increase in the T wave brought about by the cardiac arrest.

C, a few minutes later, shows the beginning of another period of right vagus stimulation. Just as the heart was arrested, the injection of 50 c.c. of Ringer's solution, which entered the syringe at 65°C., was begun. Between C and D, just two seconds of heart standstill are omitted. The first beat in D is an escape. The R wave of this beat is smaller and the S wave is larger than in other beats. The net area of QRS-T for this beat is reduced from the net area of the control. With return of heart activity later in D the reduction of the T waves is clear (compare the T waves of B). E and F are continuous with D.

A few minutes later, another control vagus stimulation was identical with A and B.

SUMMARY

It is suggested, on the basis of the experimental results of cooling or warming the endocardial surface of the dog's left ventricle, that large, upright T waves in the human electrocardiogram, together with prolongation of the Q-T interval,

may often be due to ischemic changes preponderantly involving the muscle layers at the endocardial surface of the left ventricle. The best examples of electrocardiograms of this type were obtained from patients with arterial hypertension and symptoms and signs of encephalopathy. Further study is needed before the reason for this association can be suggested.

REFERENCES

1. Ashman, R., and Byer, E.: The Normal Human Ventricular Gradient. II. Factors Which Affect Its Manifest Area and Its Relationship to the Manifest Area of the QRS Complex, *AM. HEART J.* **25**: 36, 1943.
2. Ashman, R.: A Statistical Study of the Ventricular Gradient and of the QRS Complex of the Electrocardiogram. *Arch. Inst. Cardiol. Mexico* **15**: 266, 1945.
3. Ashman, R.: The Normal Duration of the Q-T Interval, *AM. HEART J.* **23**: 522, 1942.
4. Graybiel, A., and White, P. D.: *Electrocardiography in Practice*, ed. 1, Philadelphia, 1941, W. B. Saunders Co.
5. Bayley, R. H.: The Electrocardiographic Effects of Injury at the Endocardial Surface of the Left Ventricle, *AM. HEART J.* **31**: 677, 1946.
6. Wolferth, C. C., Bellet, S., Livezey, M. M., and Murphy, F. D.: Negative Displacement of the RS-T Segment in the Electrocardiogram and Its Relationships to Positive Displacement; An Experimental Study, *AM. HEART J.* **29**: 220, 1945.
7. Pruitt, R. D., Barnes, A. R., and Essex, H. E.: Electrocardiographic Changes Associated With Lesions in the Deeper Layers of the Myocardium, An Experimental Study, *Am. J. M. Sc.* **210**: 100, 1945.
8. Boyd, L. J., and Scherf, D.: The Electrocardiogram After Injury of the Inner Surface of the Heart, *Bull. New York M. Coll., Flower and Fifth Ave. Hosps.* **3**: 1, 1940.
9. Bayley, R. H.: An Interpretation of the Injury and the Ischemic Effects of Myocardial Infarction in Accordance With the Laws Which Determine the Flow of Electric Currents in Homogeneous Volume Conductors, and in Accordance With Relevant Pathological Changes, *AM. HEART J.* **24**: 514, 1942.
10. Bayley, R. H., and LaDue, J. S.: Electrocardiographic Changes of Impending Infarction, and the Ischemic Injury Pattern Produced in the Dog by Total and Subtotal Occlusion of a Coronary Artery, *AM. HEART J.* **28**: 54, 1944.
11. Wilson, F. N., Macleod, A. G., and Berker, P. S.: The T Deflection of the Electrocardiogram, *Tr. A. Am. Physicians* **46**: 29, 1931.
12. Ward, L. S.: Abnormal Electrocardiogram Following Recovery From Paroxysmal Tachycardia, *AM. HEART J.* **31**: 645, 1946 (Earlier references in this article).
13. Byer, E., and Toth, L. A.: Electrocardiographic Effects of Changing the Temperature of the Inner Surface of the Dog's Ventricle, *Am. J. Physiol.* (In press).

THE Q_3 AND QS_3 DEFLECTIONS IN THE ELECTROCARDIOGRAM: CRITERIA AND SIGNIFICANCE

HARRY E. UNGERLEIDER, M.D., AND RICHARD GUBNER, M.D.
NEW YORK, N. Y.

ALTHOUGH numerous studies have confirmed the pathologic significance of the Q wave in Lead III, first pointed out by Pardee,¹ this sign remains a subject of inquiry and some uncertainty. Occurring preponderantly in subjects with organic heart disease, particularly coronary artery disease, Q waves conforming to Pardee's criteria of abnormality are seen also in certain normal individuals, particularly in those in whom the heart lies transversely. In order to distinguish normal from pathologic Q waves in Lead III various modifications of Pardee's criteria have been recommended.²⁻⁵ Unipolar extremity leads, simultaneous registration of multiple limb leads,⁹ and esophageal leads¹⁰ have also been employed for this purpose.

Other problems complicate the interpretation of the Q wave in Lead III. Among these are its anatomic basis; the significance of Q_3 waves where marked respiratory variation occurs; the significance of small Q_3 deflections which do not meet fully Pardee's criterion, which requires Q_3 to have an amplitude equal to 25 per cent of the amplitude of the tallest QRS in the limb leads; the propriety of accepting as a Q_3 complexes preceded in some beats by a small initial upward deflection; and the significance of the QS_3 pattern and its relation to the Q_3 .

An attempt has been made to resolve some of these questions by reviewing a large source of material which appeared to be uniquely suited for such an analysis. A total of 1,355 subjects was studied, in all of whom the history, physical examination, and teleroentgenogram were reviewed, in addition to the electrocardiogram.

The following groups comprised the study.

1. Three hundred fifty-eight persons with Q waves in Lead III which conformed to the Pardee criteria. This group included (a) 103 insurance applicants with normal hearts; (b) 120 insurance applicants with hypertension or abnormal cardiac findings, such as enlargement of the heart or organic murmurs; and (c) 135 subjects with coronary artery disease who were receiving disability benefits. Most of the latter group had a history of coronary occlusion, but none of the electrocardiographic studies were made during the acute stages of infarction.

From the Medical Department, Equitable Life Assurance Society of the United States.

Presented at the Nineteenth Scientific Sessions of the American Heart Association, San Francisco, June 29, 1946.

Received for publication Aug. 10, 1946.

2. Eight hundred persons with left axis deviation. This group was composed of (a) 239 insurance applicants who had normal hearts; (b) 261 insurance applicants with abnormal cardiovascular findings; and (c) 300 patients with coronary artery disease who were receiving disability benefits. This group of 800 subjects with left axis deviation was studied in order to establish the significance of absence of the S wave in Lead I, a finding which was found to augment the significance of a Q wave in Lead III.

3. Sixty-nine persons with a QS pattern in Lead III. This group included fifty-five insurance applicants and fourteen cardiac disability patients.

4. One hundred twenty-eight insurance applicants with small Q waves in Lead III, the amplitude of which was not equal to 25 per cent of the largest QRS deflection in the standard limb leads and did not, therefore, conform to the Pardee criterion.

Large Q Waves in Lead III.—The 358 cases with Q waves in Lead III which fulfilled Pardee's criteria were also analyzed for the presence of certain other characteristics of Q_3 and for certain accompanying findings. These characteristics and findings follow: (1) body build, in terms of overweight; (2) absence of S wave in Lead I; (3) presence of Q wave in Lead II (exceeding 1 mm. or 0.1 millivolt); (4) presence of Q wave in Lead II (exceeding 2 mm. or 0.2 millivolt); (5) slurring or notching of the QRS complex in Lead II; (6) low amplitude of the T wave in Lead II (under 2 mm. or 0.2 millivolt); (7) low amplitude of the T wave in Lead II (under 1 mm. or 0.1 millivolt); (8) inversion of the P wave in Lead III; (9) widened Q wave in Lead III (0.04 second or more in duration); (10) Q wave in Lead III (exceeding 5 mm. amplitude or 0.5 millivolt); (11) Q wave in Lead III, which equaled or exceeded 75 per cent of the amplitude of the tallest R wave in limb leads; and (12) deep inversion of the T wave in Lead III (exceeding 2.5 mm. or 0.25 millivolt).

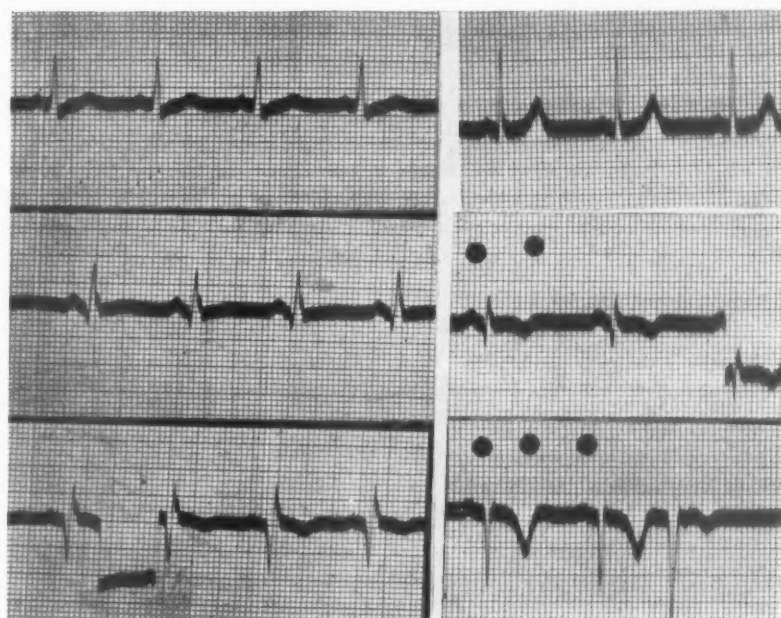
The findings are presented in Table I. The following appeared to offer a good differentiation between the "normal" Q_3 and the Q_3 due to coronary disease, since they occurred in 10 per cent or less of normal individuals with a Q_3 deflection, but were at least three times as frequent in the group with coronary disease with a Q wave in Lead III (Table I): (a) weight less than 5 per cent above normal; (b) absence of S wave in Lead I; (c) Q wave exceeding 1 mm. in Lead II; (d) low T wave in Lead II (less than 1 mm.); (e) wide Q wave in Lead III (.04 second or more in duration); (f) Q wave in Lead III, 75 per cent or more of the amplitude of the tallest R in the limb leads; and (g) deep inversion of the T in Lead III (exceeding 2.5 millimeters). (Fig. 1.)

The remaining variations studied showed definite difference in frequency of occurrence in normal subjects as compared with the group with coronary artery disease, but these criteria were less valuable in differentiating normal from pathologic Q waves in Lead III. The most significant distinguishing feature was found to be the presence of a low T wave in Lead II which occurred in only 3 per cent of normal subjects, but was present in 47 per cent of those with coronary artery disease. The presence of a Q wave in Lead II which exceeded 1 mm. was also found to be an important point of differentiation. This occurred in only

9 per cent of normal subjects, but occurred in 50 per cent of patients with coronary disease. Q waves exceeding 2 mm. were not observed in the normal group of 103 subjects, whereas they occurred in 27 per cent of the 135 patients with coronary disease. Absence of the S wave in Lead I, a sign to which no attention

 TABLE I. ASSOCIATED CHANGES OCCURRING WITH THE Q_3 DEFLECTION

	NORMAL SUBJECTS— 103 CASES (PER CENT)	CORONARY DISEASE— 135 CASES (PER CENT)	ASYMPTOMATIC HYPERTENSION OR ABNORMAL CARDIAC FINDINGS— 120 CASES (PER CENT)
1. Weight less than 5% overweight	9	36	22
2. Absent S in Lead I	10	44	27
3. Q_2 exceeding 1 mm.	9	50	18
4. Q_2 exceeding 2 mm.	0	27	9
5. QRS_2 slurred or notched	14	34	19
6. T_2 under 2 mm.	36	87	39
7. T_2 low, under 1 mm.	3	47	13
8. P not inverted in Lead III	71	88	78
9. Q_3 wide (0.04 sec. or more)	5	17	7
10. Q_3 exceeding 5 mm.	17	32	30
11. Q_3 75% or more than tallest R	6	20	9
12. T_3 inversion exceeding 2.5 mm.	2	15	3



A.

B.

Fig. 1.—Two electrocardiograms of Q waves in Lead III which exhibit associated abnormal findings: Absent S_1 (B); Q_2 exceeding 1 mm. (A and B); Low T_2 (A); Wide Q_3 (A); Q_3 equaling or exceeding 75 per cent of the amplitude of the tallest R (B); Deep inversion of T_3 , exceeding 2.5 mm. (B).

has hitherto been paid, occurred in only 10 per cent of normal subjects with Q_3 waves conforming to the Pardee criteria, while it occurred in 44 per cent of patients with coronary disease. Widening of the Q_3 wave, large amplitude of Q_3 , and deep inversion of the T wave in Lead III, while they occurred rarely in normal subjects (5 per cent, 6 per cent, and 2 per cent, respectively), were less useful as a means of differentiating normal from pathologic Q_3 waves since they did not occur with significantly greater frequency in patients with coronary disease (17 per cent, 20 per cent, and 15 per cent, respectively). The material studied was insufficient to establish absolute validity of these latter three criteria as a means of distinguishing the normal from the pathologic Q_3 .

Employing the six electrocardiographic criteria found most useful (criteria *b* to *g* inclusive of the preceding tabulation, or headings 2, 3, 7, 9, 11, and 12 of Table I), it was found that 94 per cent of the patients with coronary artery disease exhibited one or more of these abnormalities. In contrast, one or more of these abnormalities was present in 50 per cent of the group with miscellaneous abnormal cardiac findings, and in only 24 per cent of normal subjects with a Q wave in Lead III which conformed to Pardee's criteria.

The presence in the standard limb leads of one or more of the abnormalities which have just been discussed appears, therefore, to offer a satisfactory means of distinguishing the so-called normal from the pathologic Q wave in Lead III in the majority of cases. The association of such abnormalities would appear, further, to lend added significance to "indeterminate" Q waves in Lead III where an initial small upstroke precedes the initial downward deflection in some beats.

Absence of the S Wave in Lead I.—In analyzing the various electrocardiographic variations occurring with the Q wave in Lead III, it was observed that in 90 per cent of normal individuals with a Q in Lead III, an S wave was present in Lead I. In seventeen subjects with large Q waves in Lead III due to pregnancy, reported by Carr, Hamilton, and Palmer,¹¹ an S wave was present in Lead I in all instances. In contrast, in the present study S waves in Lead I were found to be lacking in fully 44 per cent of patients with a Q_3 due to coronary disease. Accordingly, a study was made to determine the significance of absence of the S in Lead I without regard to the presence of a Q in Lead III. For this purpose 800 cases with left axis deviation were studied. The source of the material was as follows: 239 insurance applicants with normal hearts; 261 insurance applicants with abnormal cardiac findings; and 300 patients with coronary artery disease who were receiving disability benefits. The findings are summarized in Table II. In normal individuals with left axis deviation, absence of an S wave in Lead I was infrequent, occurring in only 18 per cent of the subjects studied. In patients with heart disease accompanied by left axis deviation, absence of the S wave in Lead I was very frequent. It appears to be associated with left ventricular enlargement, since it occurred in 44 per cent of patients with early hypertension, and in fully two-thirds of patients with advanced hypertension who had left axis deviation. While not specific, it is by far the most frequent electrocardiographic variant accompanying left axis devia-

tion in left ventricular hypertrophy, occurring twice as often as any other electrocardiographic abnormality. Thus, in 100 patients with teleroentgenographic evidence of left ventricular enlargement which exhibited left axis deviation, an absent S wave in Lead I was observed in 64 per cent, while depression of the S-T in Lead I was present in 33 per cent, T_1 abnormalities in 30 per cent, high voltage of the QRS in 29 per cent, and other abnormalities in the ventricular complex in 27 per cent of cases.

TABLE II. ANALYSIS OF 800 CASES WITH LEFT AXIS DEVIATION, WITH REFERENCE TO S WAVE IN LEAD I

	NUMBER OF CASES	S_1 PRESENT	S_1 BORDERLINE	S_1 ABSENT
Normal heart	239	159 (67%)	36 (15%)	44 (18%)
Early heart disease				
Nonhypertensive	90	36 (40%)	14 (16%)	40 (44%)
Hypertensive	171	71 (41%)	25 (15%)	75 (44%)
Advanced heart disease				
With hypertension and enlargement				
By x-ray	100	25 (25%)	11 (11%)	64 (64%)
By electrocardiogram	100	23 (23%)	7 (7%)	70 (70%)
Coronary disease, anginal syndrome (no enlargement)	100	44 (44%)	9 (9%)	47 (47%)

It appears, therefore, that absence of the S wave in Lead I may be significant quite apart from its association with a Q wave in Lead III. However, its occurrence in 18 per cent of normal individuals with left axis deviation indicates that this sign is not a sufficiently specific abnormality to be of diagnostic value independent of other electrocardiographic findings.

The QS Pattern in Lead III.—Sixty-nine persons were studied who exhibited a QS pattern in Lead III. Of these, fourteen were cases of cardiac disability (advanced heart disease) and the remaining fifty-five were applicants for insurance. Forty-three of these fifty-five persons had heart disease or hypertension and only twelve showed no evidence of heart disease. The incidence of heart disease in persons with a QS_3 pattern (78 per cent) was considerably greater than the incidence of heart disease in an unselected group of two hundred six insurance applicants with left axis deviation (40 per cent). The occurrence of a QS_3 pattern is associated with left ventricular hypertrophy in the majority of instances. Fifty-one of the total of sixty-nine subjects with a QS_3 pattern had hypertension and electrocardiographic or roentgenologic signs of left ventricular hypertrophy.

In effect, the QS_3 pattern is equivalent to a Q_3 plus an absent S_1 . Of the sixty-nine cases with the QS_3 pattern, S_1 was absent in fifty-six cases, and in the remaining thirteen S_1 was small and did not exceed 2 mm. (0.2 mv.) in any case.

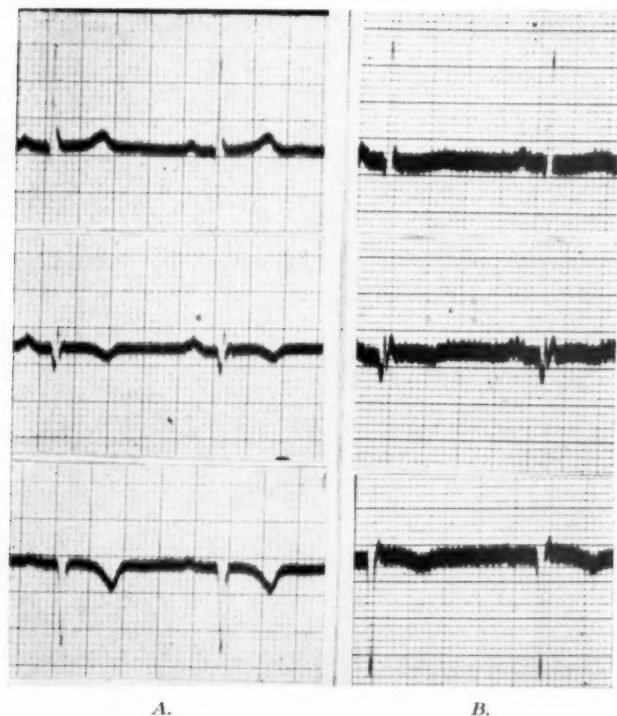


Fig. 2.—QS₃ pattern with associated Q₂. The second tracing (B) made a year following (A) shows a change from a QS₃ to Q₃ pattern.

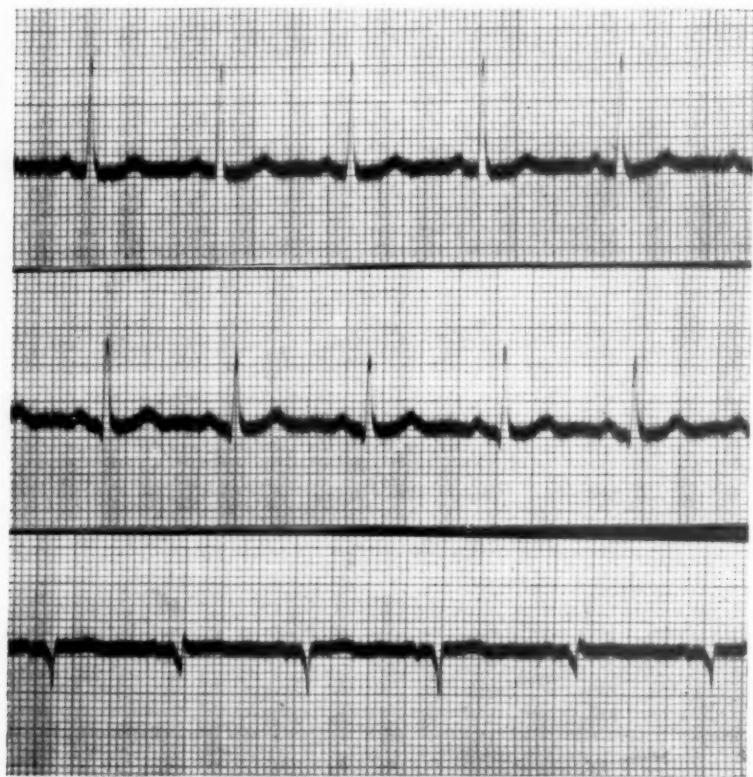


Fig. 3.—QS₃ pattern alternating with Q₃ pattern.

Evidence that the QS_3 pattern is closely related to the Q_3 pattern is seen in the frequent association of a Q in Lead II (Fig. 2), and in the transition in successive beats of the QS_3 to the Q_3 pattern (Fig. 3).

Small Q Waves in Lead III.—Analysis was made of 128 cases with a small Q_3 which did not fully conform to Pardee's criterion in that the amplitude was less than 25 per cent of the maximal QRS deflection in the limb leads. These were studied in four groups, each composed of thirty-two cases. A small Q_3 was common to all four groups. Group 1 showed, in addition, an absent S_1 with tendency to left axis deviation; Group 2, a tendency to left axis deviation (R_1 greater than R_3); Group 3, a normal electrical axis; and Group 4 showed right axis deviation. Only Group 1 (small Q_3 associated with absent S_1) showed a significantly high incidence of heart disease, nineteen of thirty-two cases. Twelve of these nineteen patients had hypertension, two died of coronary occlusion shortly after they were studied, three had an organic apical systolic murmur, one had aortic stenosis, and one patient exhibited marked T-wave abnormalities in the electrocardiogram.

These findings suggest that a small Q wave in Lead III should not be considered significant unless accompanied by an absent S wave in Lead I.

COMMENT

The employment of specialized electrocardiographic techniques, particularly unipolar extremity potentials, has contributed much to a better understanding of the Q_3 wave. It has been shown with this technique⁶⁻⁸ that the Q_3 due to myocardial infarction is the result of potentials distributed to the left leg electrode, whereas the Q_3 found in normal individuals has a different genesis. In this presentation we are stressing the desirability of attempting to obtain more definitive information concerning the Q_3 wave from the information furnished by the standard limb leads. In doing this, we have no desire to deprecate the use of specialized techniques. The present study demonstrates that differentiation of the normal from the pathologic Q_3 is usually possible if the criteria which were found to be most useful in this analysis are applied.

Several of the accompaniments of the Q_3 which add significance to this wave have been previously pointed out. These include the presence of a Q in Lead II² and an increased duration of the Q_3 .⁴ Attention does not appear to have been called, hitherto, to the added significance of absence of an S wave in Lead I, a frequent finding in the patients of this series who had heart disease. In contrast, an S wave in Lead I is generally present in persons with "normal" hearts who show Q waves in Lead III, for example, in pregnant women. Independent of an association with a Q_3 , absence of the S wave in Lead I is a relatively infrequent finding in normal individuals with left axis deviation, whereas it is extremely common in the presence of heart disease, particularly left ventricular hypertrophy. Unfortunately, this sign is not sufficiently specific to be of definite diagnostic value in itself. However, it lends added significance to the Q_3 ; even when the Q_3 is of small amplitude, the association with an absent

S_1 strongly suggests the presence of an abnormal heart. The QS_3 pattern in effect amounts to a Q_3 plus absent S_1 and is at least as significant as the deep Q_3 alone.

An attempt was made to carry out a follow-up study of mortality. However, it was possible to reinvestigate only seventeen cases who died, a number too small for statistical purposes. In all of these seventeen persons, Q_3 was the only abnormal finding on examination for insurance. The electrocardiogram was taken, in most instances, because of the large amount of insurance for which application was made. Q_3 waves of four types were included in this study: (1) Q_3 with accompanying electrocardiographic changes of significance, as indicated in the present study. There were five patients in this category, all of whom died of coronary artery disease at intervals varying from one and one-half to nine years after the electrocardiogram was made. The average survival period was 4.4 years. (2) Q_3 deflections which conformed to the Pardee criterion, but were not accompanied by other abnormalities. Five patients of the series fitted into this category. Four of these five patients died of heart disease and one died of pneumonia. The average survival period was 5.5 years. (3) Q_3 deflections which exhibited marked respiratory variation. Three of the four patients who showed this finding died of heart disease and one died of cerebral thrombosis. The average survival period was 7.1 years. (4) Small Q_3 deflections which did not fully conform to the Pardee criterion. All three patients with this type of Q wave died of heart disease. The average survival period was 6.5 years.

While no valid statistical conclusions can be drawn from such a small number of cases, the unusually high incidence of deaths from heart disease (15 of 17 cases) is striking. Even among the patients with presumably normal hearts in whom the Q_3 appeared due to transversely placed hearts and obesity, the high incidence of death from heart disease is remarkable. The full significance of these findings must await analysis of a much larger experience. However, this small sample suggests that a Q_3 is an unfavorable prognostic sign, and even in the presence of obesity, marked respiratory variations, or relatively small amplitude of the Q_3 , it becomes questionable whether this sign can be lightly dismissed as a normal variant.

Different mechanisms appear to operate in causing each of the three different types of Q deflections which may be observed in the electrocardiogram: (1) the Q wave due to infarction, (2) the small Q deflections which are observed normally, and (3) the deep Q_3 which occurs in normal subjects with horizontally placed hearts. The deep Q_3 or QS_3 frequently observed in left ventricular hypertrophy probably arises from a mechanism similar to the mechanism which produces it in horizontal position of the heart.

The mechanisms of origin of Q waves may be visualized by the schematic representations in Fig. 4.

1. In myocardial infarction, as Wilson¹² has shown, an infarct which involves the entire thickness of the ventricular wall acts as a window, so that the negativity of the interior of the ventricular cavity is transmitted directly to the surface of the body. The surface electrode, therefore, registers a potential similar

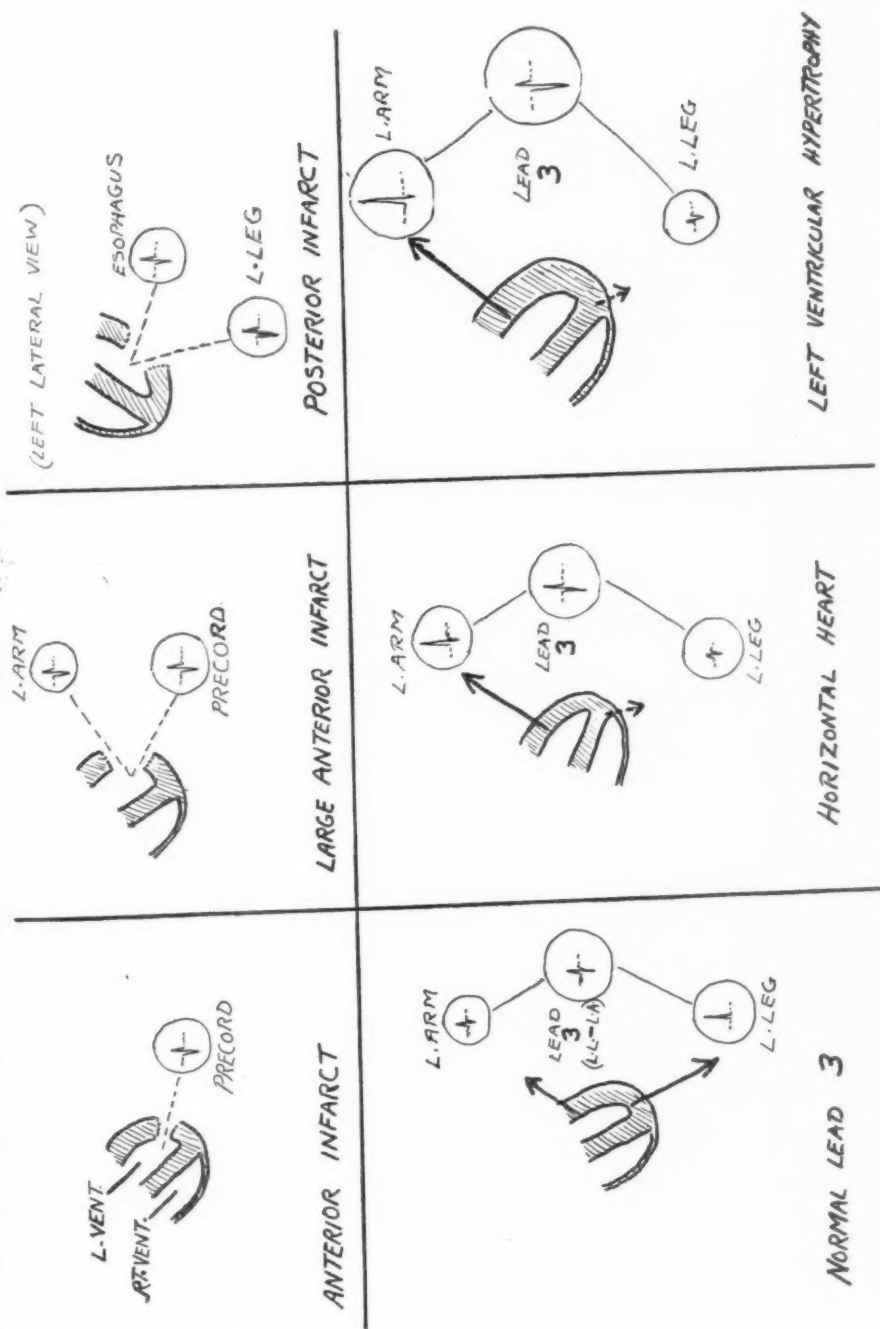


Fig. 4.—Mechanisms of origin of Q waves in infarction, in horizontal position of the heart, and in left ventricular hypertrophy. The infarct acts as a "window" so that leads in the path of the "window" act as semidirect leads from the interior of the ventricular cavity, recording the initial negative potential of the ventricular cavity. In anterior infarction this is detected by precordial leads. If the infarct is large, a deep Q will appear over a wide area of the left chest wall and also in the left arm, appearing as a Q in Lead I. In posterior infarction, the initial negative potential is transmitted to the leads from the left leg and esophagus. When the heart is transversely placed an increased positive potential is registered in the left arm lead producing greater negativity of Lead III (left leg minus left arm potential). This may appear as a deep S or deep Q in Lead III. This is further accentuated in left ventricular hypertrophy.

to that recorded by an electrode placed within the interior of the ventricular cavity. In anterior infarction, the negativity of the interior of the ventricular cavity is transmitted to leads directly over the precordium, and, when the infarct is large, to the left arm as well, resulting in a Q wave in the standard Lead I. In posterior infarction, located on the under surface and posterior surface of the heart, the negativity of the ventricular cavity is transmitted inferiorly to the left leg, and posteriorly where a Q wave may be recorded in esophageal leads.

2. The small Q deflection which is observed in persons with normal hearts is probably due to the very early activation of the left side of the interventricular septum^{13,14} with passage of the impulse from the left to the right side of the septum at a time before any other ventricular excitation occurs. Since passage of electrical activity away from a point of registration is recorded as negativity,* whereas electrical activity flowing toward a point of registration is recorded as a positive potential, leads from the left side of the septum (left arm and left leg) will exhibit a small negative deflection (Q wave), which reflects passage of electrical activity through the septum away from these points of registration on the body surface. As soon as the excitation wave reaches the lateral ventricular wall and begins passage externally a positive deflection, or R wave, succeeds the small Q in these leads.

3. The deep Q₃ seen in normal individuals with horizontally placed hearts is not a Q wave in the true sense, since it is not due to negativity of the interior of the ventricle as is the Q₃ due to infarction or the small normal Q deflection. Standard Lead III is the resultant potential of unipolar extremity leads of the left arm and left leg. Lead III expresses the potential of the left leg minus the potential of the left arm, where the potential of the left arm is expressed as a negative quantity. Therefore, the more positive the potential of the left arm and the less positive the potential of the left leg, the more negative is the excitation wave as recorded in Lead III. In the normally placed heart the direction of potential is illustrated in Fig. 4. A positive potential is transmitted both to the left leg and left arm; and Lead III (left leg minus left arm) is still positive, or slightly negative (normal left axis deviation). In the transversely placed heart (Fig. 4) a much greater positive potential is transmitted to the left arm. Only a small positive potential, or even a negative potential, is transmitted to the left leg, since the direction of the excitation to the greater part of the ventricle may be away from the left leg. The resultant Lead III (left leg minus left arm), as Myers and Oren⁷ have pointed out, may exhibit a deep S wave (left axis deviation), or even a deep Q or QS deflection. In hypertrophy of the left ventricle, the thickened left ventricle will further accentuate the degree of left axis deviation and appearance of a deep Q or QS deflection, because of the augmented positive potential in the left arm electrode.

It is seen in Table I (Column 3) that the characteristics of the Q₃ deflection in subjects with hypertension more closely resemble the "normal" Q₃ than the

*It is for this reason that the potential of the interior of the ventricular cavity is negative throughout excitation: the impulse is passing outward from the interior of the ventricular wall. In this discussion of the excitation wave only the left ventricle and interventricular septum are considered. The contribution of the thin right ventricle to the excitation wave is ordinarily small and may be disregarded.

Q_3 due to coronary disease (previous posterior infarction). The association of a large Q_3 with left ventricular hypertrophy in the absence of a history of infarction, a striking finding in the present series, has been noted previously. Thus, in autopsies on nine patients with a large Q_3 reported by Willius,¹⁵ considerable left ventricular hypertrophy was present in all but one. The fact that the hearts of four patients showed no changes in the coronary arteries was considered by Willius to support the view that left ventricular hypertrophy was the dominant factor in the genesis of the Q wave in Lead III. Similar observations were made by France.¹⁶ In twelve patients with a large Q_3 deflection on whom necropsy was performed, infarction was present in only five, whereas hypertrophy was present in all but two of the twelve.

SUMMARY AND CONCLUSIONS

An analysis of a large series of cases was undertaken to establish criteria of abnormality of the Q_3 deflection in the electrocardiogram. Certain findings appear to aid in the differentiation of the "normal" Q_3 and the Q_3 due to coronary disease. The findings which follow were found to be present in 10 per cent or less of normal individuals with a Q_3 wave conforming to Pardee's criterion. They were present at least three times as frequently in subjects with a Q_3 due to coronary disease.

- (a) Weight less than 5 per cent overweight.
- (b) Absence of S wave in Lead I.
- (c) Q wave exceeding 1 mm. in Lead II.
- (d) Low T wave in Lead II (less than 1 mm.).
- (e) Wide Q wave in Lead III (0.04 second or more in duration).
- (f) Q wave in Lead III which equals or exceeds 75 per cent of the amplitude of the tallest R in the limb leads.
- (g) Deep inversion of the T wave in Lead III (exceeding 2.5 mm.).

In order of importance the features which were most significant of an abnormal Q_3 were found to be a low T wave in Lead II, the presence of a Q in Lead II which exceeded 1 mm. in amplitude, and an absence of an S wave in Lead I. Employing the six electrocardiographic criteria (b-g), it was found that 94 per cent of patients with a Q wave in Lead III due to coronary artery disease exhibited one or more of these abnormalities, while only 24 per cent of normal subjects with a Q_3 conforming to Pardee's criterion showed one or more of these findings. The presence of one or more of these abnormalities in the standard limb leads offers a satisfactory means of distinguishing the so-called normal from the pathologic Q wave in Lead III.

Absence of the S wave in Lead I not only confers added significance to a Q_3 deflection, but may be of some significance without relation to its association with a Q_3 deflection. It appears to be associated with left ventricular enlargement, since it was present in fully two-thirds of the patients with advanced hypertension who exhibited left axis deviation. The occurrence of this finding in 18 per cent of normal individuals with left axis deviation indicates that ab-

sence of S_1 is not a sufficiently specific abnormality to be of diagnostic value of itself. While not specific, it is by far the most frequent electrocardiographic variant accompanying left axis deviation in left ventricular hypertrophy, since an absent S in Lead I occurred twice as often as any other electrocardiographic abnormality. The QS_3 pattern is closely related to the Q_3 pattern and is, in effect, equivalent to a Q_3 plus an absent S_1 . Small Q waves in Lead III, not conforming in amplitude to Pardee's criterion, are not significant unless there is also an absence of the S wave in Lead I.

A limited mortality study suggests strongly that the Q_3 deflection is a significant abnormality which should not be dismissed simply because of associated overweight and transverse position of the heart. Fifteen of seventeen cases with no cardiovascular abnormalities other than a Q_3 deflection died of heart disease, after an average survival period for the entire seventeen cases of 5.7 years. The duration of life was shortest (4.4 years) in a group of five cases in which the Q_3 pattern was accompanied by electrocardiographic findings which are indicated by this study to increase the significance of the Q_3 deflection.

Different mechanisms are concerned in the genesis of the Q_3 wave due to infarction, on the one hand, and the Q_3 and QS_3 deflection which may occur in the horizontally placed heart and in left ventricular hypertrophy, on the other. The mechanisms of origin of the normal small Q wave, the Q wave due to infarction, and the Q_3 and QS_3 deflections due to horizontal position of the heart and left ventricular hypertrophy are discussed.

REFERENCES

1. Pardee, H. E. B.: The Significance of an Electrocardiogram With a Large Q in Lead 3, *Arch. Int. Med.* **16**:470, 1930.
2. Durant, T. M.: The Initial Ventricular Deflection of the Electrocardiogram in Coronary Disease, *Am. J. M. Sc.* **188**:225, 1934.
3. Wallace, A. W.: The Q Wave in the Electrocardiogram, *Am. J. M. Sc.* **188**:498, 1934.
4. Bayley, R. H.: The Significance of the Duration of Q_3 With Respect to Coronary Disease, *AM. HEART J.* **18**:308, 1939.
5. Mazer, M., and Reisinger, J. A.: Criteria for Differentiating Deep Q_3 Electrocardiograms from Normal and Cardiac Subjects, *Am. J. M. Sc.* **206**:48, 1943.
6. Lyle, A. M.: Further Observations on the Deep Q_3 of the Electrocardiogram, *AM. HEART J.* **28**:199, 1944.
7. Myers, G. B., and Oren, B. G.: The Use of the Augmented Unipolar Left Leg Lead in the Differentiation of the Normal From Abnormal Q Wave in Standard Lead III, *AM. HEART J.* **29**:708, 1945.
8. Goldberger, E.: The Differentiation of Normal from Abnormal Q Waves, *AM. HEART J.* **30**:341, 1945.
9. Shookhoff, C., and Douglass, A. H.: The "Q" Deflection in Normal and Abnormal Human Electrocardiograms, *Ann. Int. Med.* **8**:177, 1934.
10. Nyboer, J.: The Normal and Abnormal Esophageal Electrocardiogram, With Particular Reference to Myocardial Infarction, *AM. HEART J.* **22**:469, 1941.
11. Carr, F. B., Hamilton, B. E., and Palmer, R.: The Significance of Large Q in Lead III of the Electrocardiogram in Pregnancy, *AM. HEART J.* **8**:519, 1933.
12. Wilson, F. N., MacLeod, A. G., Barker, P. S., Johnston, F. D., and Klostermeyer, L. L.: The Electrocardiogram in Myocardial Infarction, with Particular Reference to the Initial Deflection of the Ventricular Complex, *Heart* **16**:155, 1933.
13. Lewis, T.: Mechanism and Graphic Registration of the Heart Beat, ed. 3, London, 1925, Shaw & Sons, Ltd.
14. Mahaim, I.: Nouvelles Recherches sur les Lésions du Faisceau de His-Tawara, *Ann. de méd. lég.* **32**:347, 1932.
15. Willius, F. A.: The Significance of Large Q Waves in the Electrocardiogram.
16. France, R.: The Large Q Wave in Lead III of the Electrocardiogram, *Am. J. M. Sc.* **187**:16, 1934.

COMPARATIVE STUDY OF THE INTRACAVITY POTENTIAL IN MAN AND IN DOG

DEMETRIO SODI PALLARES, M.D., MARIO VIZCAINO, M.D., JORGE SOBERON, M.D.,
AND ENRIQUE CABRERA, M.D.
MEXICO, D. F., MEXICO

THERE is very little literature on cardiac intracavity potentials recorded with unipolar leads. Wilson and associates,¹ working on dogs, were the first to point out that the left intraventricular record shows an exclusively negative QRS complex (complex QS). In the intracavity record of the right ventricle, there may appear an initial positivity (R wave) preceding the great negative complex. This positive deflection has been attributed to septal activation. Wilson and co-workers² described the changes in the shape of the intraventricular records after the production experimentally of bundle branch block. When there is left bundle branch block, the negativity disappears from the left cavity and the record is that of the RS type; the right cavity potential is exclusively negative (QS). If the block is produced on the right side, the left intraventricular potential remains exclusively negative (QS), and that from the right cavity is of the RS type. One of us³ studied in dogs the modification of the negative intracavity potential in the left ventricle after ligation of the anterior descending artery. Wolferth and associates⁴ studied the displacement of the RS-T segment of intracavity records in different experimental conditions. They did not find displacement of that segment after the ligation of the coronary vessels. Lenegre and Maurice⁵ described the intracavity leads in the right auricle and ventricle of the human heart. Recently, Hecht⁶ studied the morphology of the intracavity tracings recorded from the right auricle and ventricle and analyzed the results on the basis of the dipole theory. We know of no other publication related to the intracavity potentials obtained with unipolar leads.

This study was undertaken to amplify our knowledge of the intracavity potential. It embraces (1) the intracavity potential of the dog in different experimental conditions (the four cavities of the heart were studied) and (2) the potentials of the right cavities of the human heart, in normal and pathologic conditions.

THE INTRACAVITY POTENTIAL OF THE DOG

The following points were studied:

1. Left intraventricular potential after ligation of the anterior descending artery (with particular reference to displacement of the RS-T segment).

Read at the Inter-American Congress of Cardiology, Mexico, D. F., Oct. 5-12, 1946.
From the National Institute of Cardiology of Mexico.

2. Left intraventricular potential after ligation of the left circumflex artery (with special reference to the RS-T segment).
3. Right and left intraventricular potentials during the production of ventricular extrasystoles.
4. Intracavity potentials in right bundle branch block.
5. Intracavity potentials in left bundle branch block.
6. Intraventricular potentials in complete heart block.

Material and Method.—The experiments were carried out in dogs under nembutal and urethane. The anesthetic solution (50 Gm. of urethane dissolved in distilled water to which 20 Gm. of nembutal were added to 200 c.c. of water) was injected intraperitoneally (1 c.c. per 3 kilograms of body weight). Artificial respiration was given either by tracheotomy or by tracheal intubation with a Foregger catheter. In all dogs the heart was widely exposed by opening the chest down the mid-line, from the xiphoid appendix to the interclavicular symphysis.

After opening the pericardium, the serous membrane was sutured to the costal wall in order to form a cradle for the heart. The electrodes used were similar to those already described by one of us.³ The silver chloride intracavity electrodes were sometimes covered with cotton. Records were taken from the epicardium by attaching the cotton wicks of the electrodes to the epicardium by means of thin threads, being very careful not to damage the underlying muscle. For the intracavity leads, the electrodes were introduced through the auricular appendix. Since the left auricular appendix, lying toward the back, is difficult to reach, it is convenient to open a window in the costal wall in order to make the operations easier. Some of the records from the right cavities were obtained by introducing a special electrode through the femoral vein into the heart. In many of the experiments it was possible to control the intracavity position of the electrode by feeling it through the muscular wall. At the end of the experiment the position of the electrode was always verified.

The left circumflex artery was ligated near the origin of the vessel. The anterior descending artery was ligated before it begins to branch.

In order to sever the right bundle branch, a thin knife was introduced through the right ventricular wall, near the auriculoventricular sulcus, at a point between the emergence of the anterior descending artery and the right auricular appendix. It is very important to note that the point of the instrument must be directed toward the interventricular septum at an angle of approximately 45 degrees to the horizontal line. The incision, following Lewis's method,⁷ was made just beneath the septal segment of the tricuspid valve. For a depth of 2 mm. the incision should be 0.5 cm. long.

The section of the left bundle branch is technically more difficult than that of the right. The knife must be introduced in the angle formed by the left anterior descending artery and the diagonal branch one. Afterward, when the blade is inside the left ventricular cavity, it is directed toward the aortic ostium, being slipped near the interventricular septum in order to avoid the obstacle constituted by the internal leaflet of the mitral valve. It is helpful for the in-

vestigator to place the index finger of the left hand at the base of the heart, at the sulcus formed by the right auricular appendix and the posterior face of the aorta, and to direct the knife toward that finger. When the pressure of the knife is felt by the index finger through the aortic wall, the instrument is at a point above the aortic semilunar valve; the knife is then lowered a little in order to make the section. By means of this operation, it is also possible to perform the total division of the bundle of His in order to get complete heart block.

In order to avoid severe hemorrhage, a small suture can be made in the place where the knife is introduced; generally, however, compression of the wound is sufficient, as the myocardial muscular tone causes hemostasis.

All the records obtained directly from the heart were taken with unipolar leads; the indifferent electrode was placed on any of the legs. They were always standardized so that 3 mv. produced a 2 mm. deflection.

Left Intraventricular Potential After Ligation of the Anterior Descending Artery, With Special Reference to Deviation of the RS-T Segment: One of us³ has stated that the form of the intracavity potential in the left ventricle is practically unmodified by the ligation of the anterior descending artery. On that occasion the possibility was suggested that the position of the exploring electrode in relation to the injury zone might have been inadequate to register the shift. We have already said that Wolferth and associates⁴ did not find any deviation of the RS-T segment of the intracavity records after ligation of the coronary vessels.

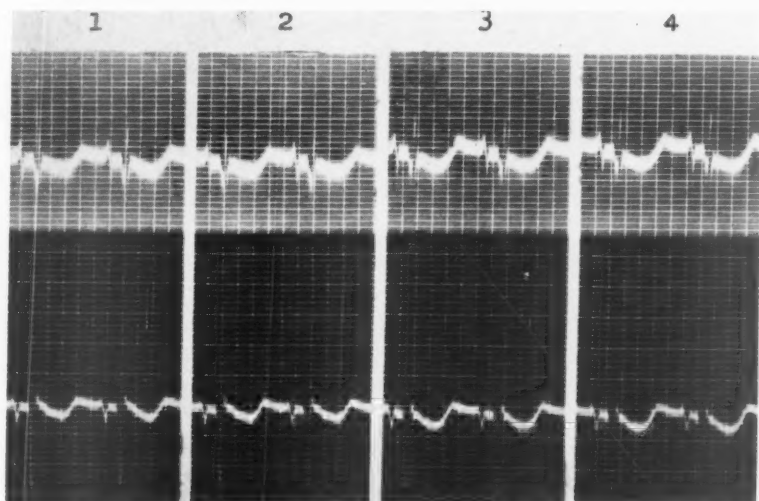


Fig. 1.—Unipolar intracavity tracings after ligation of the anterior descending artery. The upper row shows the tracings obtained when the exploring electrode was in contact with the posterior surface of the heart on a point opposite the infarction. The lower row shows the left intraventricular tracings, taken ninety minutes (1), one hundred minutes (2), one hundred ten minutes (3), and one hundred twenty minutes (4) after the ligation. Notice the negative displacement of the RS-T segment in both tracings.

After several experiments, we concluded that the negative results (thus far obtained) were due to the special position of the exploring electrode in relation to the zone of injury. This view was confirmed when we found that ninety minutes after ligation of the anterior descending artery we could obtain a negative displacement of the RS-T segment in the left intraventricular tracing (Fig. 1). Tracings taken from the posterior epicardial surface of the left ventricle show a downward displacement of the RS-T segment similar to that of the endocardial pattern (Fig. 1). In the post-mortem study we were able to prove that the intracavity exploring electrode was on the posterior surface and opposite the infarcted zone. This situation explains the striking resemblance of the RS-T patterns in the intracavity and extracavity tracings. The negative results obtained by some authors are easily explained if we take into consideration the difficulties of controlling the exploring electrode. The data can be explained according to the ideas of Bayley,⁸ which relate them to a vector directed from the center of the affected ventricle to the center of the injured zone. When the intracavity electrode is opposite to the zone of the infarction, the injury potential (RS-T) registered by it, is negative, because it is oriented toward the negative pole of the vector. Epicardial potentials of the posterior surface with a similar orientation have the same morphology as those of the intracavity pattern. Anterior epicardial potentials in the injury zone are positive and of greater voltage. On different occasions we have found (in post-mortem examinations) that the exploring electrode was in contact with atrioventricular valves. In this position its direction is nearly perpendicular to the spatial axis of injury; in such instances it is very difficult to record the shift of RS-T.

Left Intraventricular Potential, After the Ligation of the Left Circumflex Artery, With Special Reference to the RS-T Segment: In this type of experiment changes in the RS-T segment were very easily obtained, in contrast to the results of the experiments in which the anterior descending artery was ligated. These changes were mainly of two types.

1. In a minority of the cases there was positive displacement of RS-T in tracings made from the epicardial surface of the zone of infarction. On the other hand, the endocardial variations were not conspicuous. In Fig. 2, the upper records are epicardial and were registered in the zone of infarction. The control shows a RSR type complex, in which the second upward component is smaller than the preceding components, with negative T wave and a rise of the J point. After the ligation, positive displacement of the RS-T segment is observed, the voltage of the negative T wave decreases, and S disappears. In the control intracavity pattern, QRS is mainly negative and there is a slight positive deviation of RS-T, probably caused by pressure of the exploring electrode on the subendocardial muscle; there is no negative T wave. After the ligation, the positive RS-T deviation decreases and a negative T wave of 3 mm. is recorded. The intracavity tracing does not change in other characteristics. We suppose that in this experiment the exploring intracavity electrode was wrongly oriented with relation to the infarct, and because of this the deviation was not registered.

2. In a majority of the cases, the changes were amazing; they were characterized by a positive displacement of RS-T in the intracavity pattern and depres-

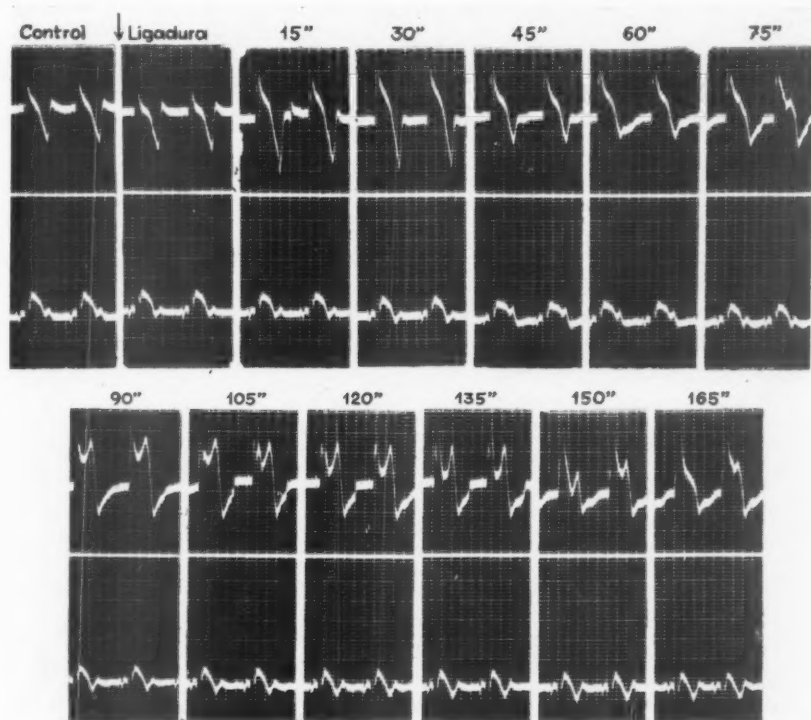


Fig. 2.—Unipolar tracings taken before and after the ligation of the left circumflex artery. The epicardial tracings (upper row) were taken from the site where the infarction was expected to appear and show the characteristic changes of an infarct: T wave waxing, positive RS-T displacement, and T wave waning. The intracavity tracings (lower row) show a positive displacement of the RS-T segment on the control; thereafter the RS-T displacement diminishes and the T wave becomes negative.

sion in the epicardial pattern (Figs. 3 and 4). The axis of injury in this type of infarct has a direction opposite to that determined by the ligation of the anterior descending artery, from which we infer that in dogs the left circumflex artery is more extensive in the subendocardial muscle than in the subepicardial.

In the upper records of Fig. 3, the exploring electrode was situated on the posterior surface of the heart. The lower records are intraventricular. The control was registered an hour and one-half after the ligation of the anterior descending artery. Afterward, at the moment indicated by the arrow, the left circumflex artery was also occluded. The time registered in the upper parts of the records indicates the moment at which the patterns were obtained after the occlusion of the circumflex artery. The cavity patterns after the second ligation show positive displacement of the RS-T, coincident with a negative shift of the epicardial pattern (at 55"). Later, the epicardial patterns have the shape of left bundle branch block; however, it is very improbable that this type of block exists because the intracavity potential is not of the RS type. The deflections become more and more bizarre until ventricular fibrillation appears.

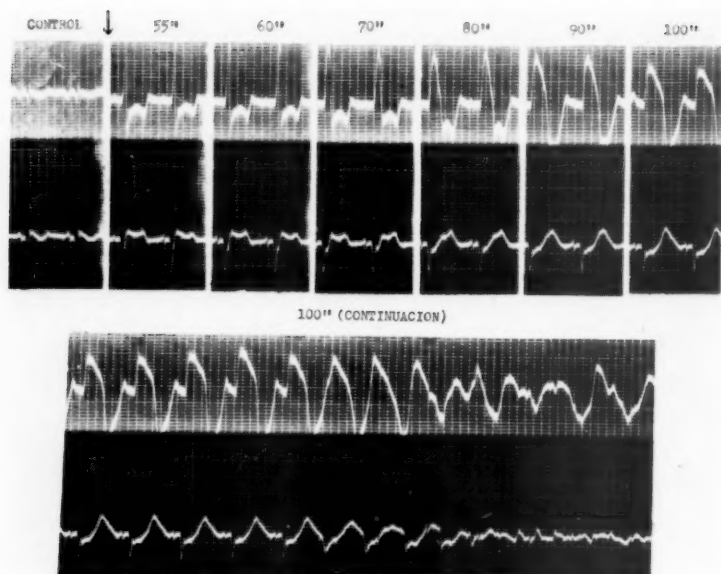


Fig. 3.—Unipolar tracings taken from the posterior surface of the heart (upper row) and from the left ventricular cavity (lower row). Control after ligation of the anterior descending artery. After the control tracing was made, the left circumflex artery was also ligated. Notice the positive displacement of the RS-T segment in the intracavity leads, coincident with negative displacement in the epicardial leads. After 70'', both tracings show changes which become more and more accentuated until ventricular fibrillation appears.

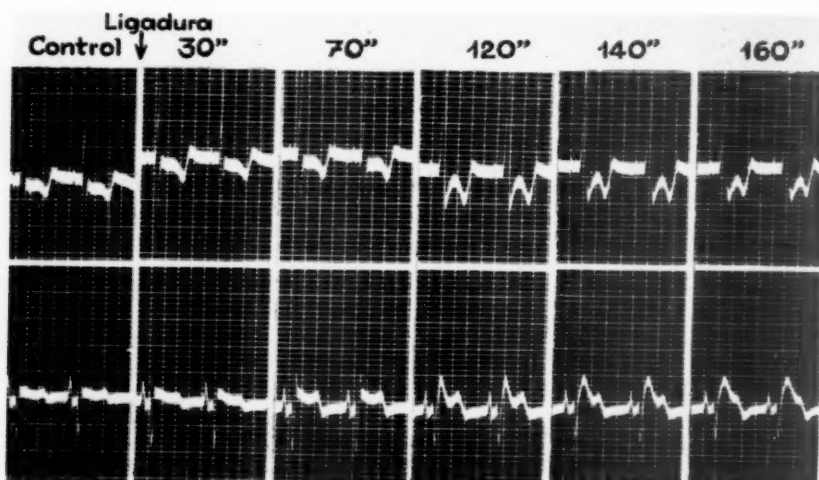


Fig. 4.—Unipolar tracings before and after the ligation of the left circumflex artery. The epicardial leads (upper row), taken from the posterior surface of the heart, show a deeper displacement of the RS-T segment. The left intraventricular leads (lower row) show a further positive displacement of the RS-T segment.

Right and Left Intraventricular Potentials During the Production of Ventricular Extrasystoles: After preparing a dog and introducing the exploring electrode into the left ventricular cavity, extrasystoles were produced by mechanical excitation at different points on the anterior surface of both ventricles. In Fig. 5 are sketched the points that were mechanically excited. Records 1, 3, 4, and 8 correspond to right ventricular extrasystoles; hence the excitation process spread

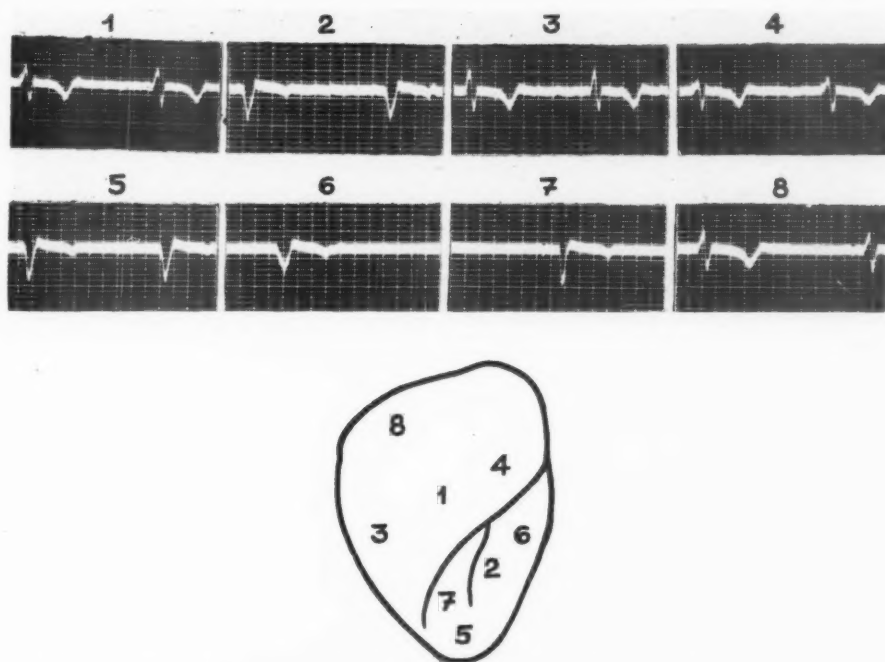


Fig. 5.—Unipolar leads from the left ventricular cavity, taken during mechanical excitation of the epicardial points indicated on the drawing. Whenever the right ventricle was stimulated, diphasic complexes of the RS type were obtained. The stimulation of the left ventricle produced a negative initial deflection.

from the right to the left heart and the QRS is of the RS type, first positive and afterward negative. The T wave is negative. The duration of QRS varied around 0.10 second. The records in Fig. 5, 2, 5, 6, and 7, correspond to left ventricular extrasystoles; here the excitation process spread from the left to the right heart, and therefore the QRS complexes are essentially negative without an initial positive phase. The T wave is slightly negative. The duration of the ventricular complex approximated 0.10 second.

In Fig. 6 the intracavity patterns correspond to the right ventricle. Whenever the excitation was produced in this ventricle, the intracavity curves were negative (lower curves of 1, 2, and 3); short crises of ventricular paroxysmal tachycardia were observed. When the excitation came from the left ventricle, the initial deflections of the extrasystolic intracavity curves was always positive. These results accord with a basic principle of the dipole theory, namely, that

the excitation wave conceived as a dipole determines a positive potential at the points which it approaches and a negative potential at the points from which it withdraws. The form of the pattern is the result of all the vectorial forces produced and depends mainly on the general direction of the excitation process and

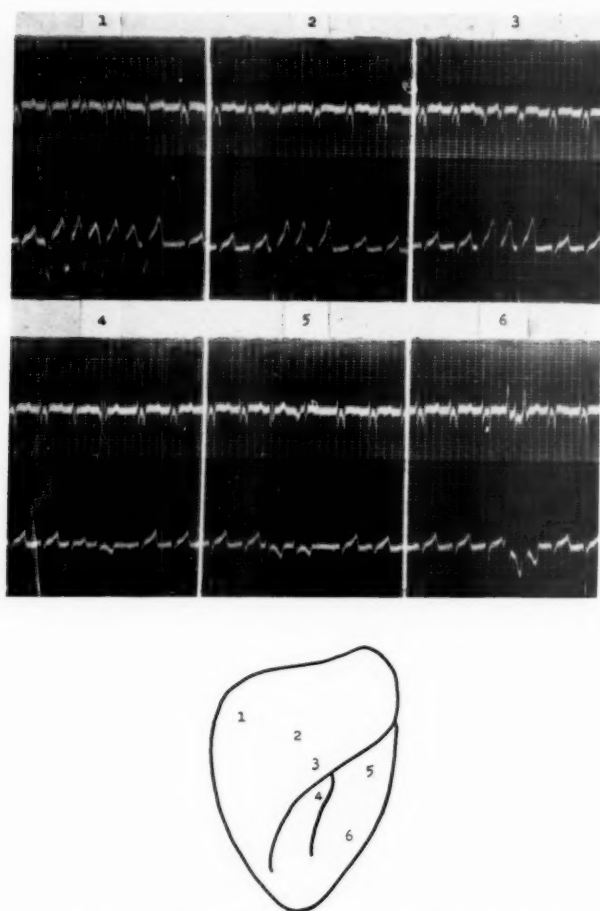


Fig. 6.—The pattern of ventricular extrasystole in the intracavitary leads. Unipolar epicardial leads, taken from the posterior surface of the heart (upper row), and unipolar right intraventricular leads (lower row). Whenever the right ventricle was stimulated (1, 2, and 3), the intracavity leads showed negative deflection. When the left ventricle was stimulated (4, 5, and 6) a positive initial deflection was obtained.

not on isolated forces originated at a given moment, as Nahum and Hoff⁹ claim. These authors, in failing to find any differences between the extrasystoles originating in the endocardium and those originating in the epicardium, differ from the opinions of Wilson and co-workers¹⁰ concerning the potential produced by the passing of the wave from the endocardium to the epicardium. Our experience, in general, supports the fundamental points proposed by Wilson, particularly with reference to the average of the excitation process.

Intracavity Potentials in Right Bundle Branch Block: Our results are very similar to those described by Wilson. After cutting the right branch of the bundle of His, the morphology of the right intracavity pattern is of the RS type (Fig. 7, 2, and Fig. 8). The production of block was tested by the morphology of Lead I

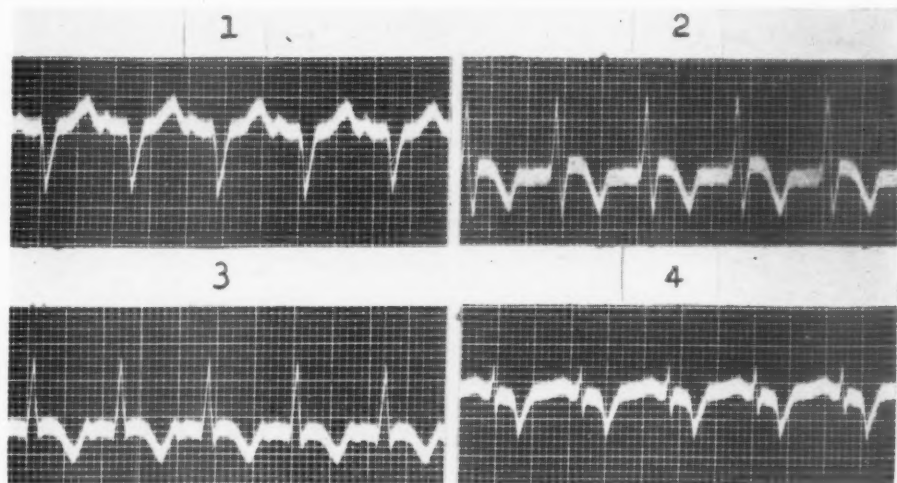


Fig. 7.—Different tracings after cutting the right bundle branch. 1, Lead I; 2, right intraventricular lead; 3, right intra-auricular lead; 4, left intra-auricular lead.

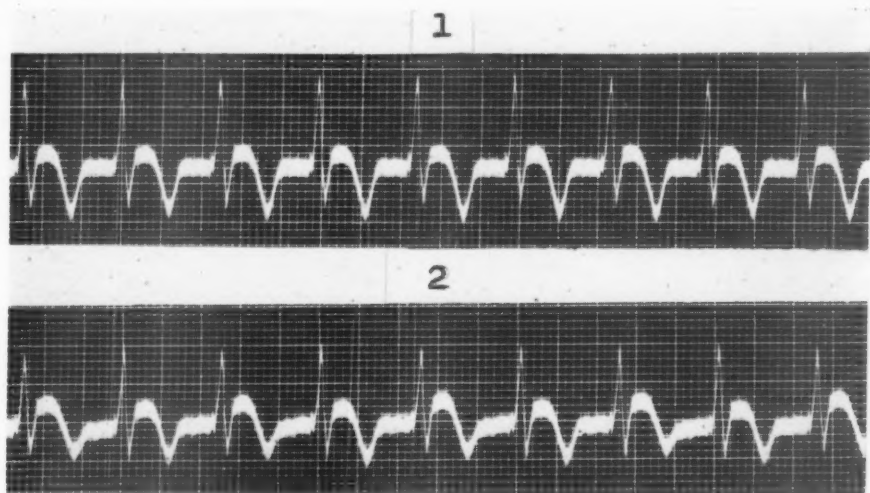


Fig. 8.—1, Right intraventricular lead after cutting the right bundle branch; 2, the same lead three minutes after the ligation of the anterior descending artery.

(Fig. 7, 1) and by the patterns registered over the epicardial surface of both ventricles (Fig. 9). All the records from the right ventricle show high R waves, delayed intrinsic deflections, and negative T waves. In the tracings obtained

from the left ventricle, the R waves are small, their peaks appear early, and the T waves are not negative. In our patterns some of the assertions of Wilson are mathematically corroborated, such as the opposition between the direction of the T wave and the larger surface of QRS and the value of the intrinsic deflection.

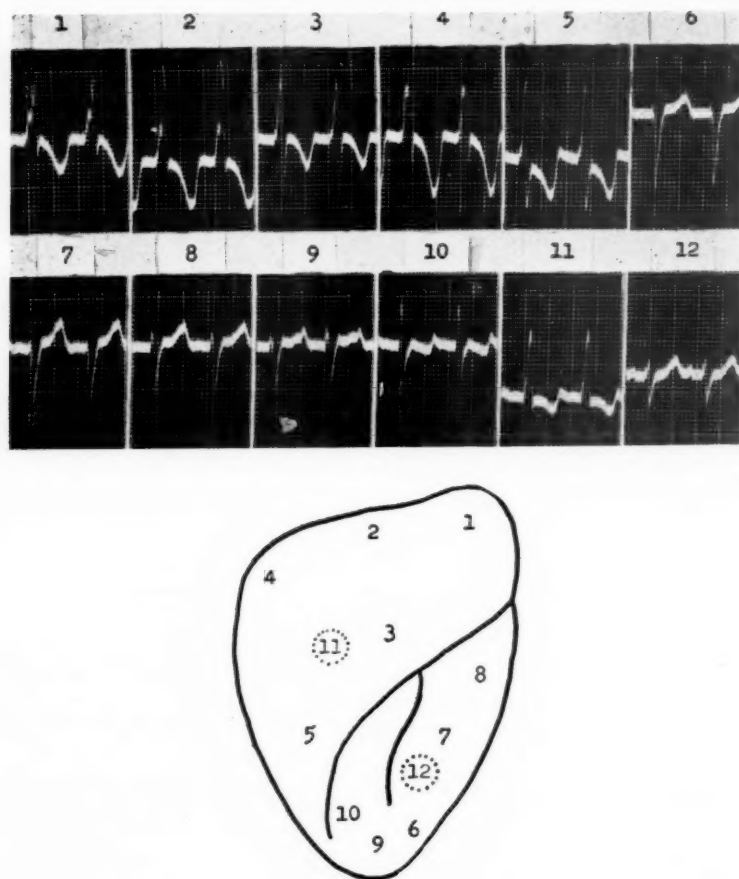


Fig. 9.—Unipolar leads taken from the epicardial surface after cutting the right bundle branch. Tracings taken from different points as indicated by the drawing. The two last points are from the posterior aspect of the heart.

Right intraventricular tracings obtained in cases of right bundle branch block are strikingly similar to those obtained in the same ventricle in cases of left ventricular extrasystoles. Both are of the RS type with negative T waves.

The right intra-auricular tracings in right bundle branch block show a ventricular complex of the qRs type with negative T waves (Fig. 7, 3, and Fig. 10, 1) and resemble left intra-auricular tracings associated with left bundle branch block (Fig. 14, 4). The normal intra-auricular tracing is of the Qr type, with a large Q and small R wave (Fig. 14, 3).

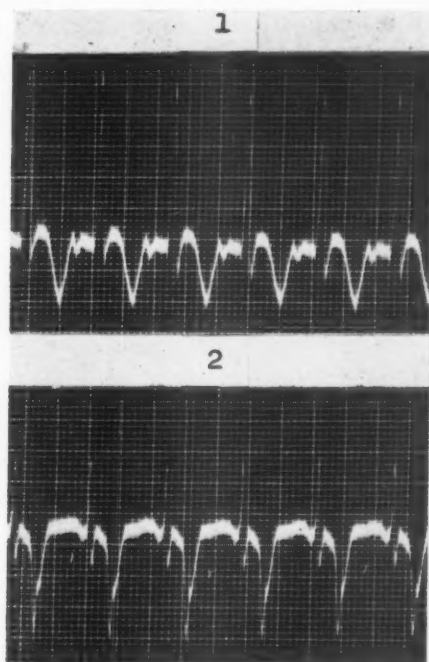


Fig. 10.—1, Right intra-auricular potential after severing the right bundle branch; 2, left intra-auricular potential in the same condition.

Intracavity Potentials in Left Bundle Branch Block: When the block is produced the left intraventricular control potential, which is negative (Fig. 11, 2), assumes an RS configuration (Fig. 11, 4) with a form similar to that found in tracings made from the right ventricular cavity when right bundle branch block is present, and from the left ventricular cavity when right ventricular extra systoles are present (compare Fig. 11, 4, with Fig. 5, 1, 3, 4, and 8 and with Fig. 8). In our left intraventricular pattern of left bundle branch block the T wave is negative. The right intracavity potential is not modified in its general form but may show slurrings (Fig. 12, 3). In this tracing the T wave becomes positive. The most favorable lead in which to verify the production of block is Lead I (Fig. 11, 3, Fig. 12, 2, and Fig. 14, 2).

In one of the experiments (Fig. 13), incomplete A-V block, 6 to 1, was produced, with left bundle branch block. The intraventricular potential shows the characteristic form (RS) of this type of block. Lead I is also characteristic.

In Fig. 14 the intra-auricular potentials are shown before and after cutting the left branch of the bundle of His. The left intra-auricular control tracing (Fig. 14, upper tracing of 3) shows an essentially positive P wave with a QRS complex of the QR type with a small, positive T wave. After the branch is cut, the P wave remains unchanged and the QRS complex turns into the qRs type with a negative T wave (Fig. 14, upper tracing of 4). The right intra-auricular control tracing (Fig. 14, lower tracing of 3) shows an essentially negative P wave

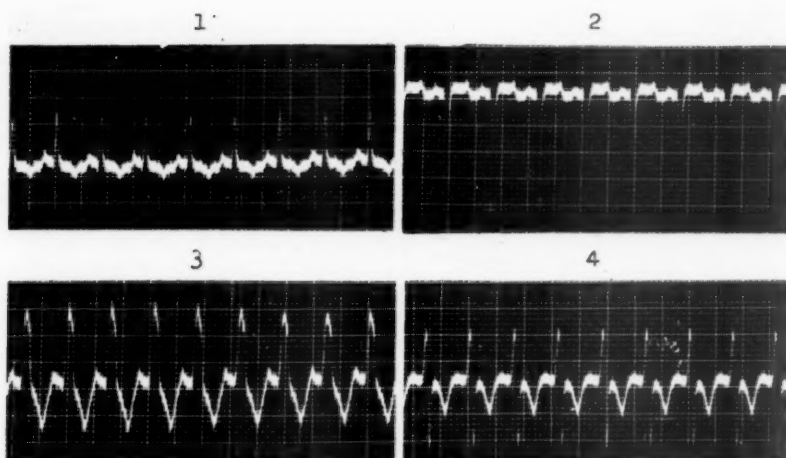


Fig. 11.—Experimental left bundle branch block. 1, Lead I, control; 2, left intraventricular potential, control; 3, Lead I after cutting the left bundle branch; 4, left intraventricular potential after cutting the left bundle branch.

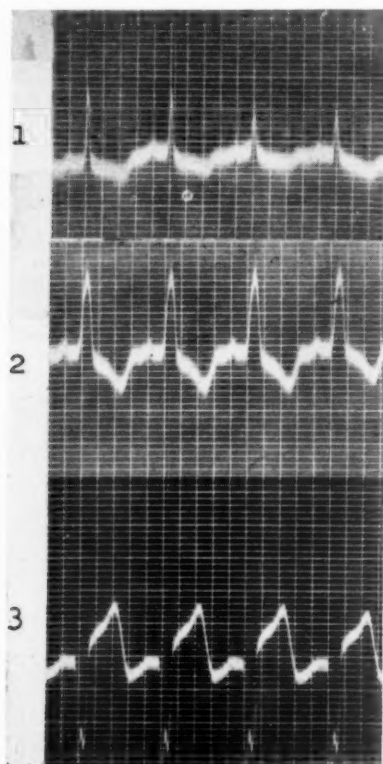


Fig. 12.—Experimental bundle branch block. 1, Lead I, control; 2, Lead I after cutting the branch; 3, right intraventricular potential after cutting the left bundle branch.

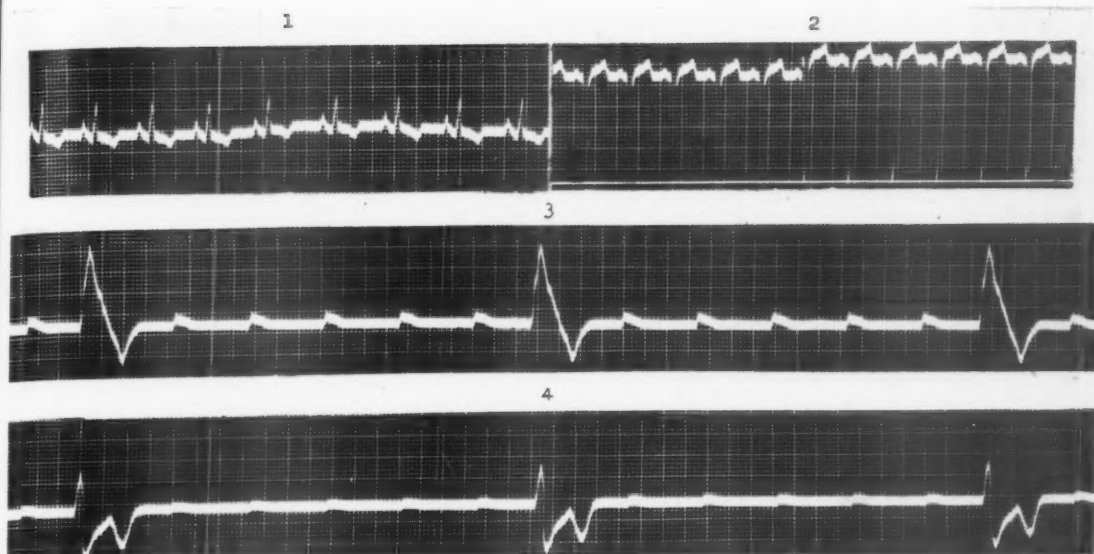


Fig. 13.—1, Lead I, control; 2, left intraventricular lead, control; 3, Lead I showing incomplete A-V block (6 to 1) and left bundle branch block; 4, left intraventricular potential showing the same changes.

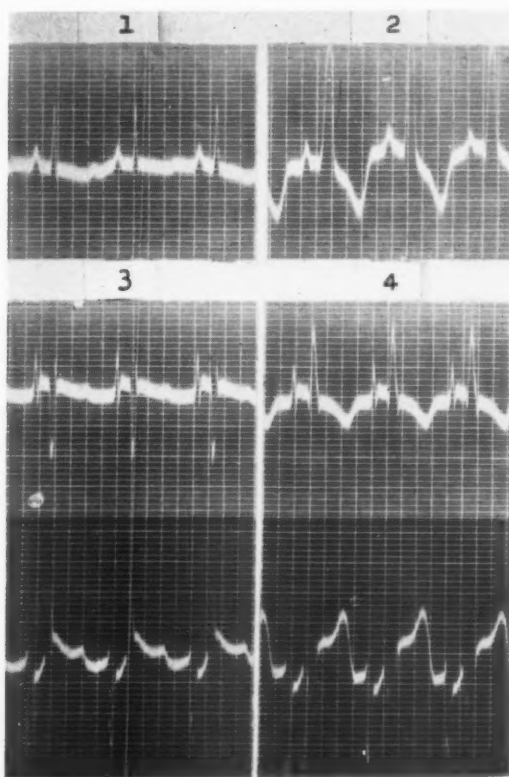


Fig. 14.—1, Lead I, control; 2, Lead I after cutting the left bundle branch; 3, left intra-auricular potential (upper tracing) and right intra-auricular potential (lower tracing), control; 4, the same leads after cutting the left bundle branch.

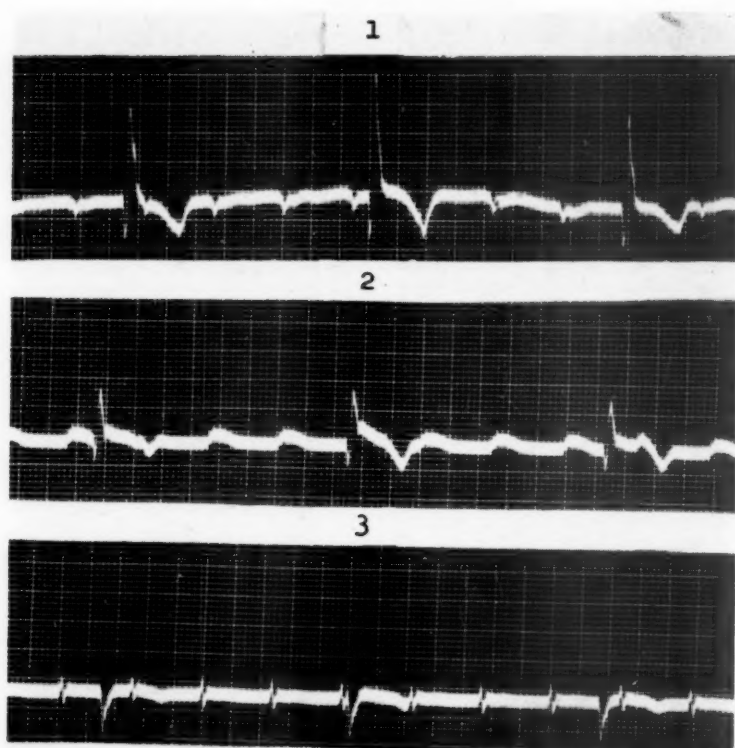


Fig. 15.—The effect of cutting both branches of the bundle of His. 1, Lead I; 2, right intraventricular potential; 3, left intraventricular potential.

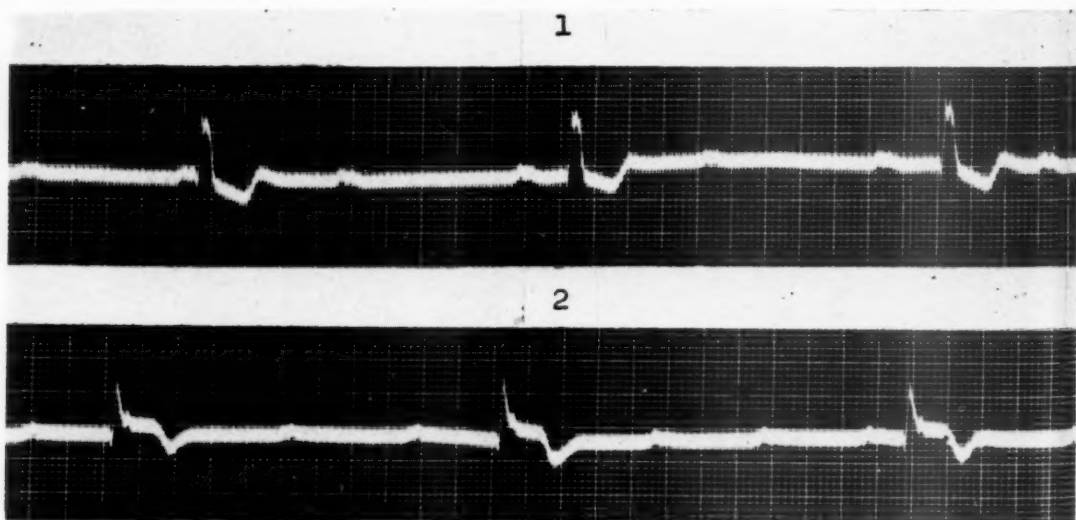


Fig. 16.—Complete A-V block with idioventricular rhythm simulating a left bundle branch block, after cutting the bundle of His. 1, Lead I; 2, left intraventricular lead.

with a ventricular complex of the QR type; when the branch is cut, the P wave remains unchanged and the ventricular complex becomes the QS type with notchings. In this tracing the T wave increases its positive potential (Fig. 14, lower tracing of 4).

Intraventricular Potentials in Cases of A-V Block: With A-V block and an idioventricular rhythm, the shape of the pattern is variable and depends on the site at which the ventricular stimulus originates. Thus in Fig. 15, the form of the right intraventricular pattern is of the QR type and that of the left ventricle is exclusively negative (QS), which suggests that the ectopic rhythm begins in the left ventricle. It is possible to confuse Lead I of Fig. 16 with left bundle branch block, but the two are differentiated by the facts that a Q wave is present in Lead I and that the QRS complex in the left intraventricular pattern is of the QR type and not the RS type which results from cutting the left branch.

THE RIGHT INTRACAVITY POTENTIAL OF THE HUMAN HEART

Six normal subjects and twenty patients with heart disease were studied. The exploring electrode was like that used in the animal experiments and was introduced through the right (less frequently through the left) external jugular vein. After local application of novocain, the vein was isolated. The introduction of the electrode was controlled by fluoroscopy. The indifferent electrode was attached to any one of the limbs. In almost every case the standardization of the galvanometer was such that 1 mv. produced a deflection of 2 millimeters. All patients received a small dose of barbiturate. In one case it was necessary to give intravenous ouabain because of paroxysmal dyspnea. In another case, the presence of the electrode in the ventricular cavity brought on chest pain that disappeared shortly after the electrode was retracted. Still another patient complained of a vague pain in the back of the chest and right shoulder, coincident with the recording of a monophasic wave, while the catheter was in contact with the ventricular endocardium. When the catheter was retracted, the patient presented a short run of ventricular extrasystoles and the monophasic wave disappeared. Every patient received a prophylactic treatment of penicillin for two days after the operation and follow-up was continued for one month afterward. None of the patients showed any lasting ill effects.

The Normal Electrocardiogram of the Intracavity Leads.—

P Wave: The shape of the P wave is variable, depending upon the position of the exploring electrode. When this is in the superior vena cava or near the sinus node, the P wave (Figs. 17 and 18) is exclusively negative (PQS according to Hecht's terminology). Its amplitude is greater when the electrode is near the sinus node than when it is in the vena cava.

When the electrode is in the center of the auricle, the P wave is diphasic (Fig. 19, C) of the plus-minus type (PRS). The preponderance of the positive or negative phase depends upon the distance of the exploring electrode from the sinus node. Sometimes the P wave has a small initial negativity (PQRS), which could be attributed to irregular distribution of the wave of excitation leaving the

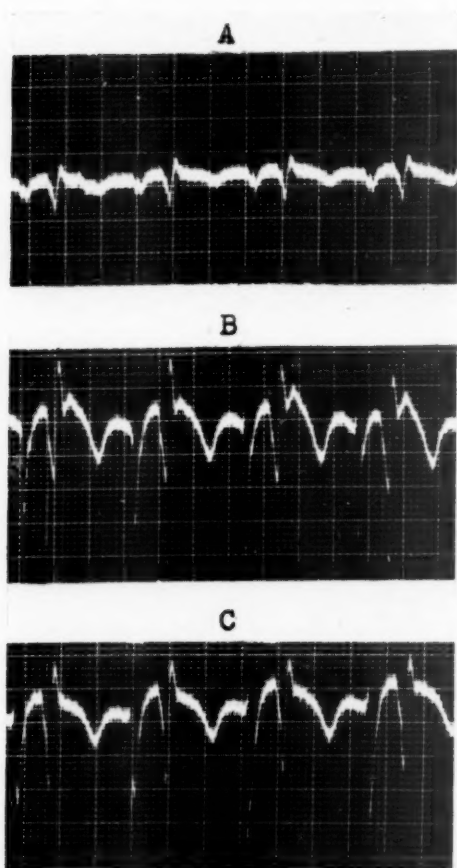


Fig. 17.—Normal intracavity potential. A, Superior vena cava; B and C, high auricular level.

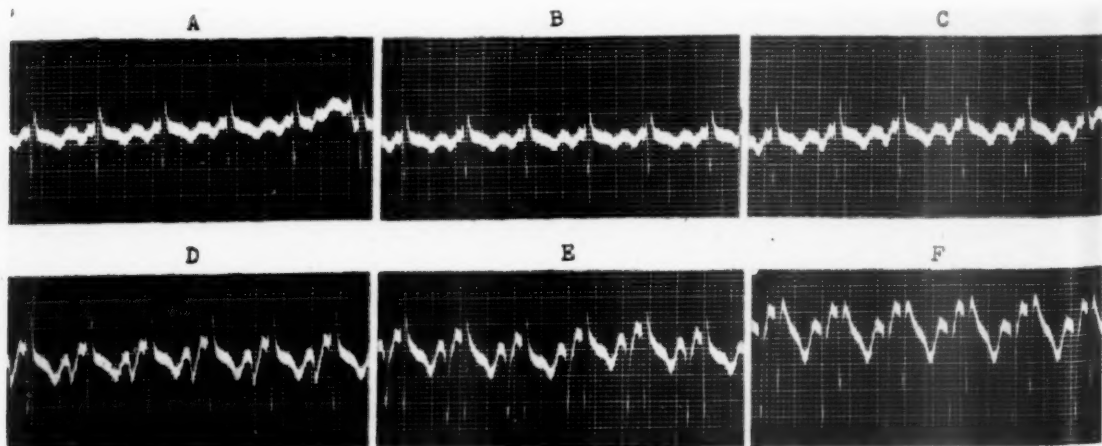


Fig. 18.—Normal intracavity potential. Unipolar tracings from: A, B, C, and D, superior vena cava, at different levels; E and F, high auricular level.

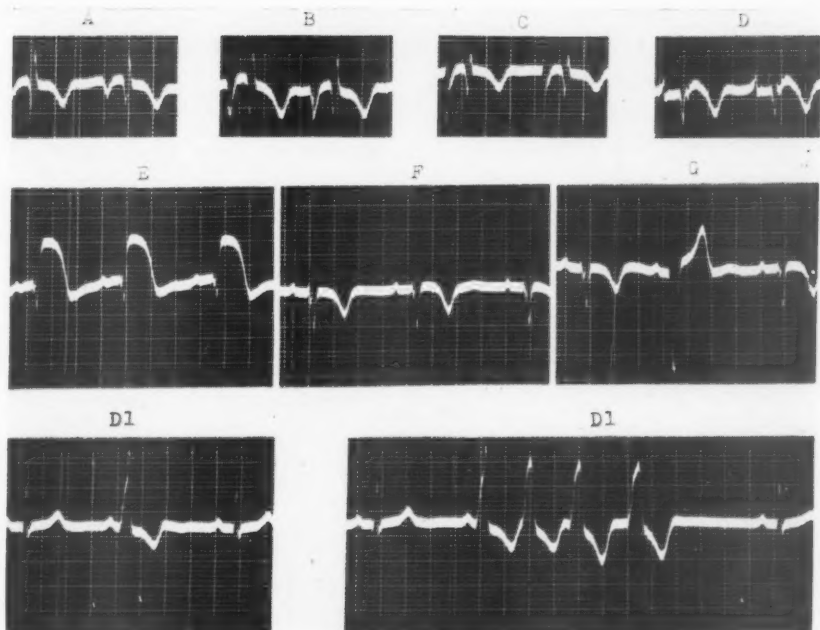


Fig. 19.—Right ventricular extrasystoles. Unipolar tracings from: *A*, superior vena cava; *B*, high auricular level near the sinus; *C*, mid-auricular level; *D*, *E*, *F*, and *G*, ventricular cavity.

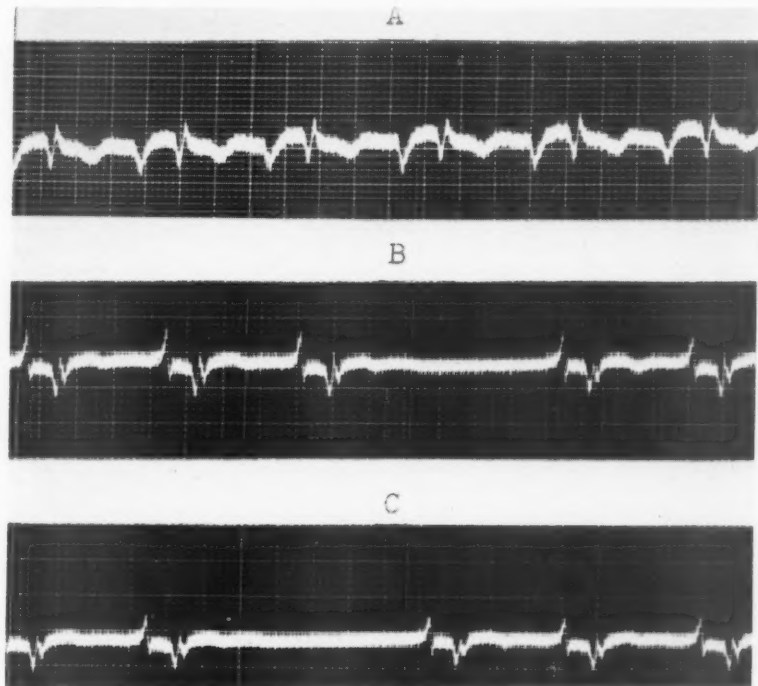


Fig. 20.—Sinoauricular block. Unipolar tracings from: *A*, high auricular level, near the sinus node; *B* and *C*, low auricular level.

sinus node, resulting, at a given moment, in predominance of the forces leaving the exploring electrode (Fig. 22, B).

When the electrode is in the lower part of the auricle, the P wave is exclusively positive or diphasic (Fig. 20, B and C) with a definite preponderance of the positive phase (PRs). In the inferior vena cava or the right ventricular cavity, the P wave is exclusively positive and of lower voltage. In a few instances when the electrode is in the inferior vena cava, the P waves are of high voltage (Fig. 24, E and F).

The shape of the auricular wave is in accordance with a principle of the dipole theory: when the wave of excitation approaches a point, this point becomes positive; when it leaves a point, this point becomes negative.

If the pacemaker is not in the sinus node but in the A-V node, the auricular potentials become reversed; that is, positive at the level of the sinus and negative at the level of the A-V node. Fig. 21 shows a shifting of the pacemaker from the sinus to the A-V node which resulted in a shortening of the P-R interval from 0.15 to 0.10 second. The exploring electrode at the level of the sinus detected a negative P wave when the P-R interval was 0.15 second, and a positive P wave when it was 0.10 second; the ventricular complex was slightly modified.

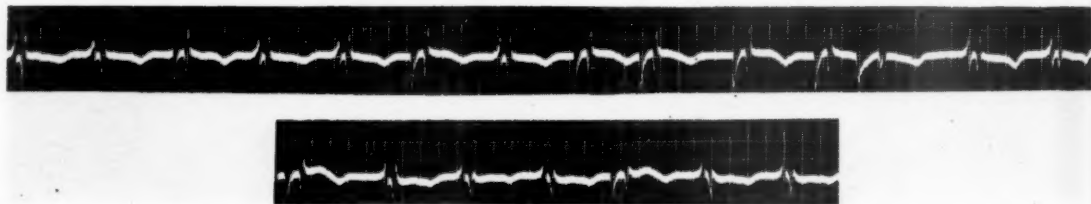


Fig. 21.—Wandering pacemaker. Continuous tracing from a high auricular level, near the sinus node. The negative P wave (during sinus rhythm) becomes positive when the pacemaker shifts to the A-V node.

Ventricular Complex: The ventricular complexes taken from the auricular cavity are always predominantly negative, and may be of the QR, QRS, rSR' or rS type (Figs. 17, 18, 19, 20, 21, and 35). At high and middle auricular levels, the two first types, QR and QRS, are more frequent; at lower auricular levels and near the septum, the two latter types, rSR' and rS, are more common. We speak of a "late R" when the ventricular complex is of the QR or QRS type and of an "early R" when the complex is of the rS type; when the complex is of the rSR' type, we call the first positive wave "early R" and the second positive wave "late R."

In the experiments in animals we found that the voltage of the late R in the right auricular cavity was modified by section of any of the branches of the bundle of His. The voltage increased when the right branch was cut, and the late R disappeared when the left branch was cut. For this reason we assume that the late R is due to late activation of certain portions of the right ventricle.

The early R obtained at lower auricular levels is attributed by us to septal activation. No such wave is found at the upper levels, probably because the

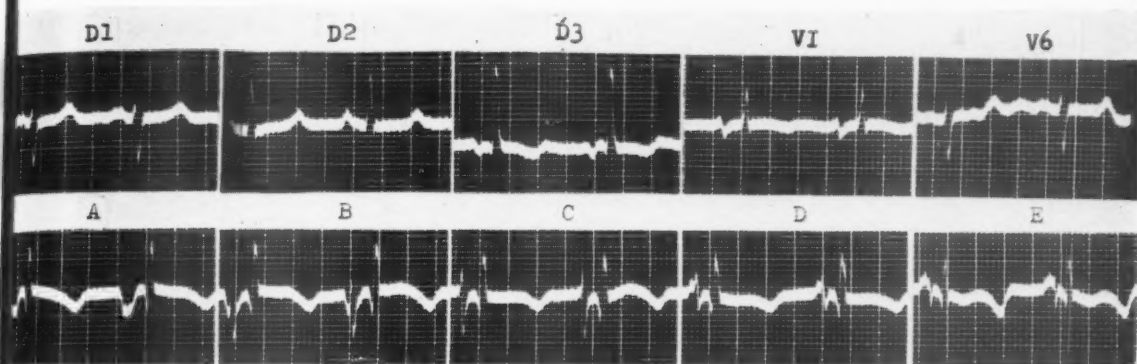


Fig. 22.—Right ventricular hypertrophy. Unipolar tracings from: A, high auricular level near the sinus node; B, high auricular level near the mid-auricle; C, mid-auricular level; D and E, low auricular levels.

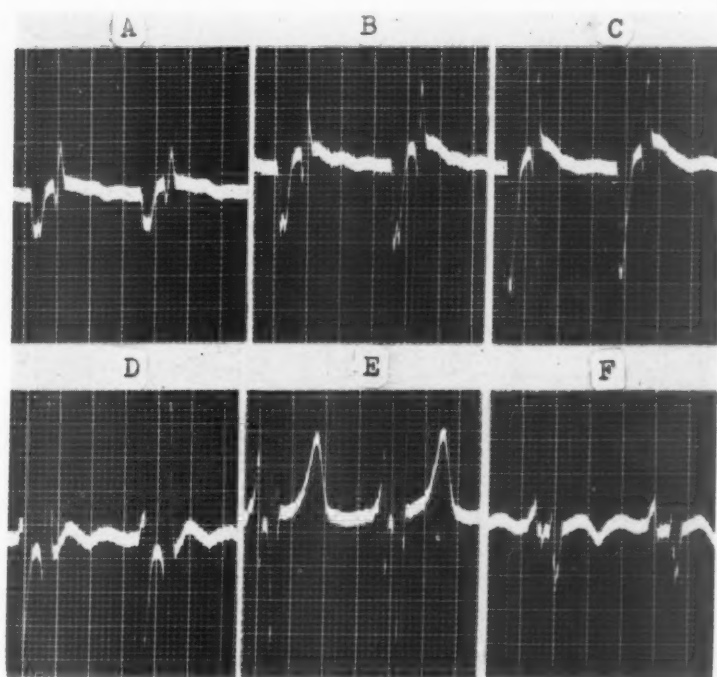


Fig. 23.—Right ventricular hypertrophy. Unipolar tracings from: A, superior vena cava; B and C, auricular cavity near the sinus node; D, high auricular level; E, mid-auricular level; F, low auricular level.

exploring electrode lies in a perpendicular line with the vector which indicates the activation of the ventricular septum.

The negative deflections of the ventricular complexes found in the auricular cavity are probably due to activation of the free walls of both ventricles.

In the right ventricular cavity the ventricular complex is commonly of the rS type. We attribute the R wave to septal activation and the S wave to activation of the free walls of both ventricles (Fig. 19, *F* and *G*; Fig. 32, *A*; Fig. 33, *D*).

Right Ventricular Hypertrophy: The general form of the P wave is similar to that found in normal subjects, but these waves tend to be slurred and notched. The QRS complex in intra-auricular tracings is also similar but with different voltage of its deflections: negative components, Q and S, predominate over the R waves in the normal subjects and the R waves are greater than the Q and S waves in patients with hypertrophies. In other words, positive deflections predominate in right ventricular hypertrophy (Figs. 22, 23, and 24). It seems logical to assume that the high R wave of right ventricular hypertrophy is due to the late activation of some hypertrophied muscular portions of the right ventricle.

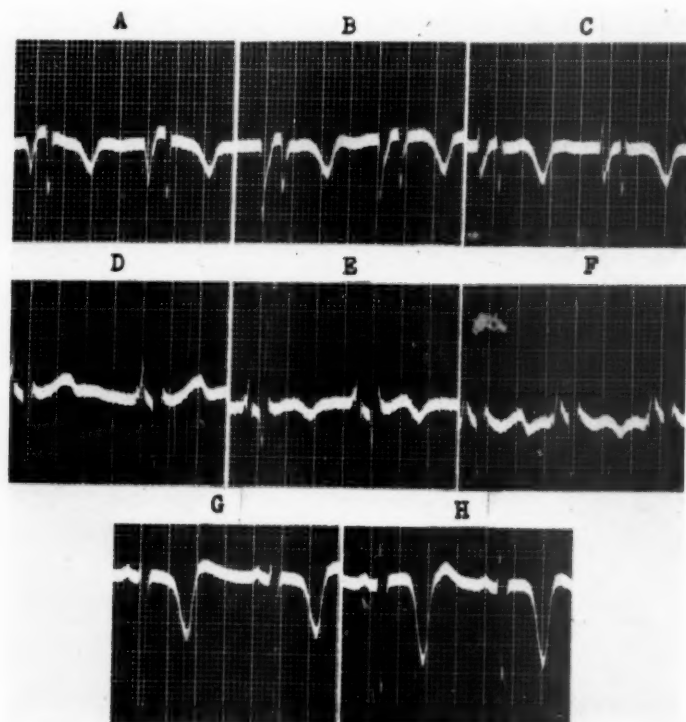


Fig. 24.—Right ventricular hypertrophy. Unipolar tracings from: *A*, superior vena cava; *B*, auricular cavity near the sinus node; *C*, mid-auricular level; *D*, low auricular level; *E* and *F*, inferior vena cava; *G*, ventricular cavity; *H*, same cavity near the pulmonary conus.

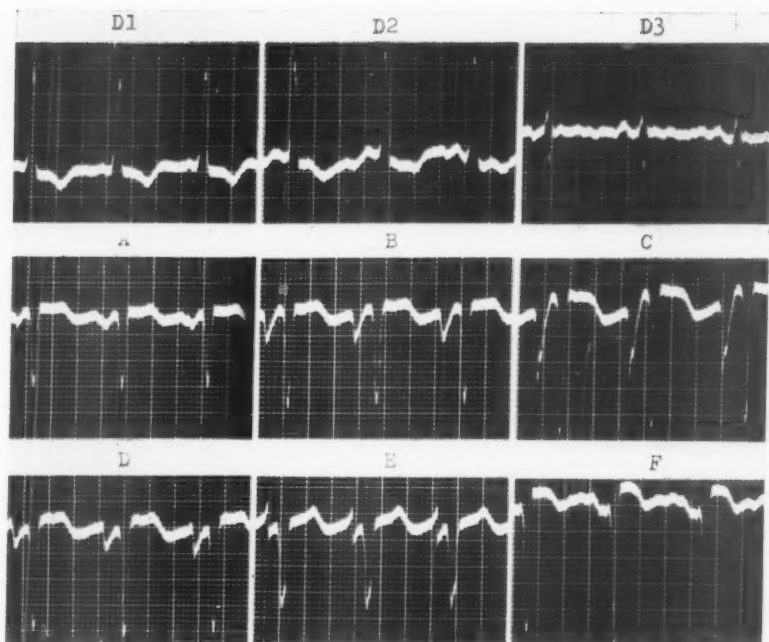


Fig. 25.—Left ventricular hypertrophy. Unipolar tracings from: *A*, superior vena cava; *B*, auricular cavity near the sinus node; *C* and *D*, high auricular level; *E*, low auricular level; *F*, ventricular cavity.

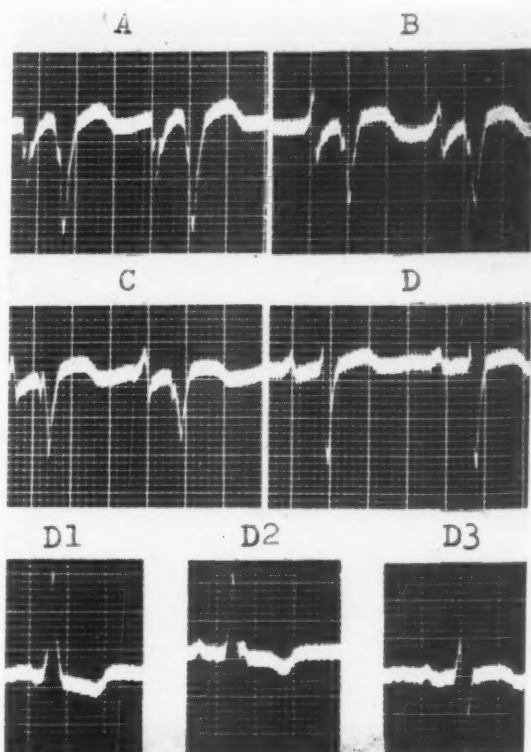


Fig. 26.—Left ventricular hypertrophy. Unipolar tracings from: *A*, auricular cavity near the sinus node; *B*, mid-auricular level; *C*, low auricular level; *D*, ventricular cavity.

In the right ventricular cavity, the tracing is similar to the normal: rS (Fig. 24, *G* and *H*). The first positive deflection which is small, appears early and may be attributed to septal activation. The negative deflection, which is larger, may be ascribed to the activation of the free walls of both ventricles.

In one patient with pulmonary emphysema and chronic cor pulmonale (Fig. 24, *H*) the catheter was introduced up to the pulmonary conus. There the early R was higher than in any other part of the right ventricle. This may be a normal finding or it may have been due to hypertrophy of the upper part of the septum.

Left Ventricular Hypertrophy: The P wave is similar to that found in normal subjects. The ventricular complexes are almost the same at any level in the auricle: of the QS or QRS type; that is, with negative deflections predominating (Fig. 25, *B*, *C*, *D*, and *E*; Fig. 26, *A*, *B*, and *C*; Fig. 27, *A*, *B*, and *C*).

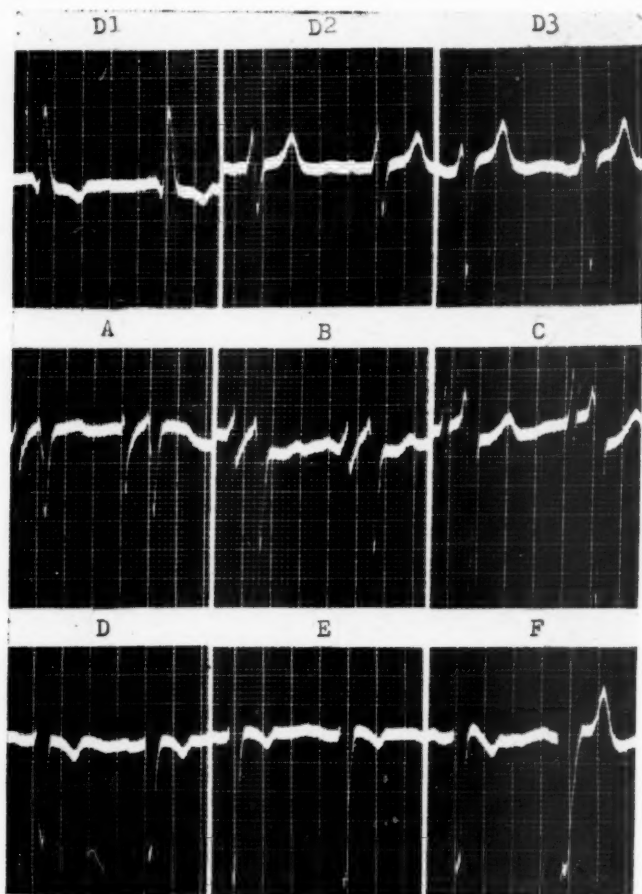


Fig. 27.—Left ventricular hypertrophy. Unipolar tracings from: *A*, high auricular level; *B*, mid-auricular level; *C*, low auricular level; *D*, *E*, and *F*, ventricular cavity.

The late R is either small or absent, probably because of the opposition of the forces of the hypertrophied walls of the left ventricle. This occurs also in left bundle branch block in animals and men. The intraventricular tracing was always of the rS type (Fig. 25, *F*; Fig. 26, *D*; Fig. 27, *D*, *E*, and *F*), generally with a positive T wave.

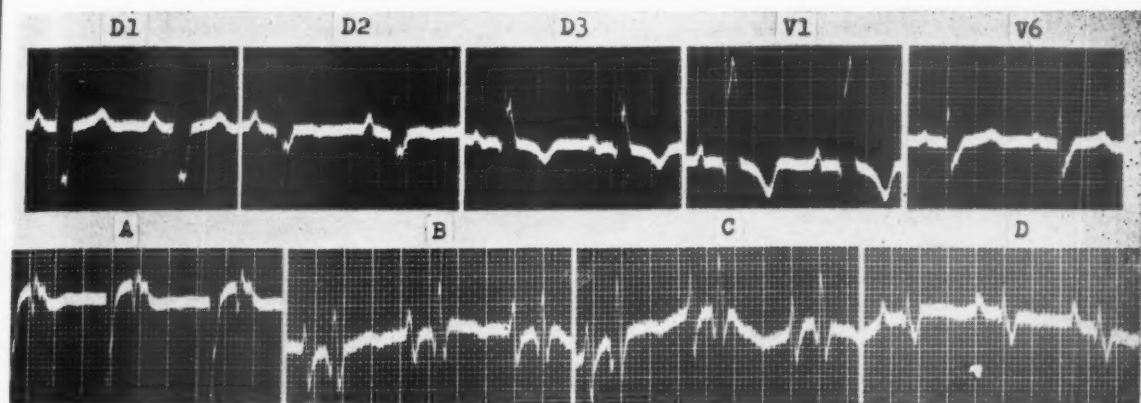


Fig. 28.—Right bundle branch block. Unipolar tracings from: *A*, high auricular level; *B* and *C*, mid-auricular level; *D*, inferior vena cava.

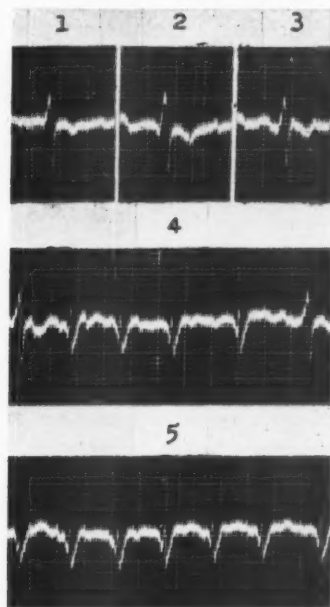


Fig. 29.—Unipolar right intraventricular leads in cases of right bundle branch block. Notice the typical plus-minus form of the QRS complex (*1*, *2*, and *3*) and the small run of right ventricular extrasystoles produced by the contact of the exploring electrode (*4* and *5*).

In one of our patients (Fig. 27, C) the early R was higher in the lower part of the auricle than in the right ventricle. This may be ascribed to hypertrophy and bulging of the upper part of the septum.

Right Bundle Branch Block: The intra-auricular QRS complexes are similar to those found in right ventricular hypertrophy, with a definite preponderance of positive deflections (Fig. 28, A, B, and C).

At the upper part of the auricle, the late R is broad and slurred (Fig. 28, A) like that found in Lead VR in the same condition. At the lower part of the auricle the late R is still predominant but less slurred (Fig. 28, B and C). The tracing is strikingly similar to that found in experimentally produced block in the dog. One case (Fig. 28) had the same shape in Lead V₆ and in the tracing obtained from the inferior vena cava.

The intraventricular tracing (Fig. 29, 1, 2, and 3) shows diphasic QRS complexes (of the RS type) with negative T waves and is more or less like the tracing obtained from the right ventricular cavity in experimentally produced right bundle branch block and left ventricular extrasystoles.

Left Bundle Branch Block: The P wave shows no changes. The QRS complex in tracings made with the electrode in the lower auricle presents purely negative (QS) deflections (Fig. 30, A, B, and C). In tracings made from the upper part of the auricle (Fig. 30, A) the complex is of the W type, but its ascending portion does not go above the isoelectric line; therefore, strictly speaking, they are QS complexes with splinterings.

It is important to remember that the normal auricular tracings in both man and the dog show a late R. In the dog this wave disappears when the left branch is severed; in man a late R is not found in left bundle branch block.

In tracings made from the ventricular cavity, there is a deep QS complex (Fig. 30, D and E), without the initial positivity described by Hecht.⁶ The auricular as well as the ventricular tracings present a positive T wave with positive displacement of the RS-T segment.

In Fig. 31 are shown the tracings obtained inside the cavities of the right heart in normal cases, in ventricular hypertrophy, and in two types of bundle branch block.

Ventricular Extrasystoles.—In several of the experiments, the mechanical action of the exploring electrode brought on premature ventricular beats (Figs. 19, 27, 29, and 32) or even short runs of ventricular paroxysmal tachycardia (Figs. 19 and 29). At times these premature beats could be produced at will. These beats evidently arose from the right ventricle. The intraventricular tracings always showed a QS complex while the first lead showed exclusively positive complexes. The T wave was always opposite in direction to the QRS deflection. The form of these tracings is very similar to that of experimentally produced right ventricular extrasystoles in animals and to that of left bundle branch block in both men and animals.

Miscellaneous Conditions.—Some other conditions were incidentally studied and are presented here.

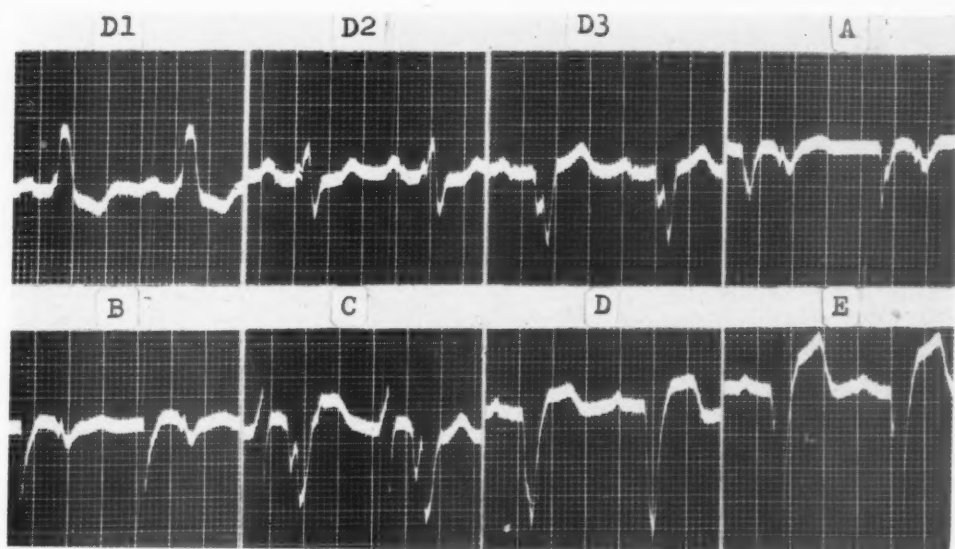


Fig. 30.—Left bundle branch block. Unipolar tracings from: A and B, high auricular levels near the sinus node; C, mid-auricular level; D and E, ventricular cavity.

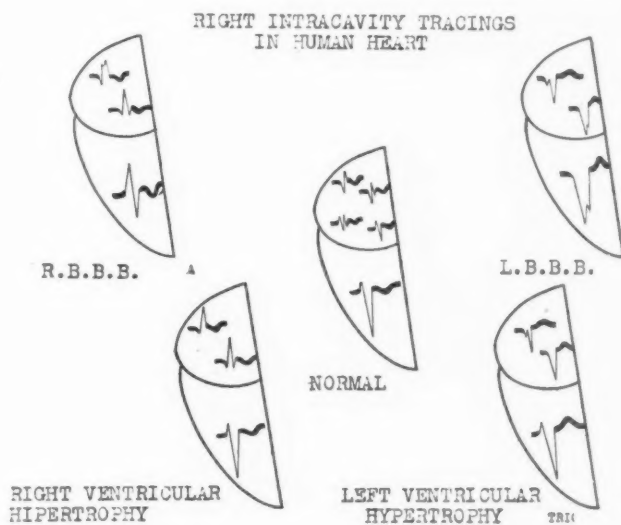


Fig. 31.—The right intra-auricular and intraventricular tracings in different conditions.

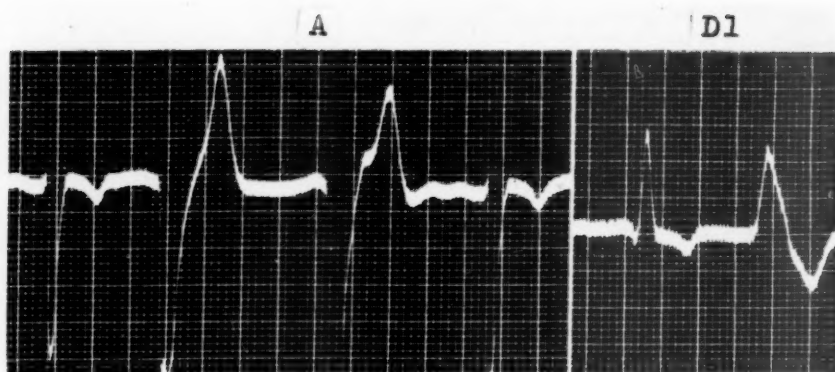


Fig. 32.—Right ventricular extrasystoles. *A*, right intraventricular tracing. Notice the negative (QS) complex and the positive T wave of the premature beats; *B*, in Lead I, the aspect of the premature beat is like that of left bundle branch block.

Subendocardial Ischemia (Fig. 33): One of our patients with clinical angina pectoris developed a squeezing chest pain radiating to the neck and left shoulder while the record was being taken. The T wave, which previously had a negative amplitude of -14 mm. (Fig. 33, *E*), became more negative with an amplitude of -22 to -25 mm. (Fig. 33, *F*). The R wave did not change. It is logical to assume that a subendocardial ischemia appeared or became accentuated.

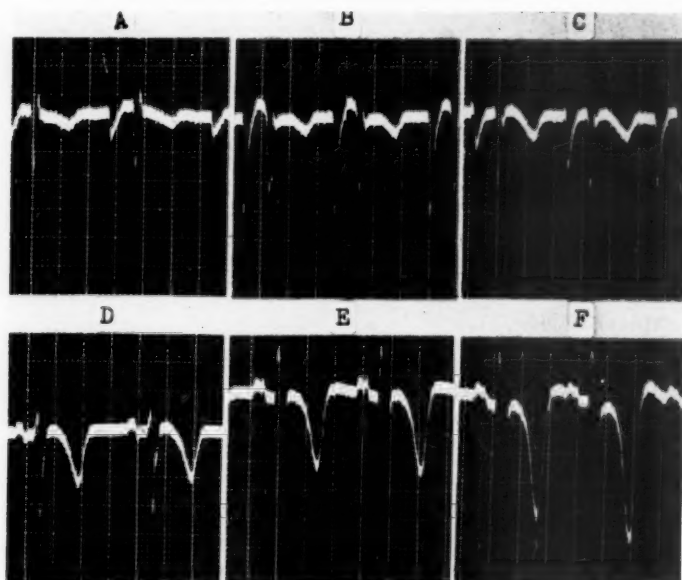


Fig. 33.—Subendocardial ischemia. Unipolar tracings from: *A*, superior vena cava; *B*, auricular cavity, near the sinus node; *C*, high auricular level; *D* and *E*, intraventricular tracings; *F*, the same as (*E*) after the appearance of a severe precordial pain; notice the waxing of the T wave.

Auricular Flutter: In one case with auricular flutter and probably complete A-V block we found (1) typical flutter waves with a rate of 300 per minute, (2) ventricular rate of 36 per minute, and (3) occasional cycles of ventricular escape (Fig. 34).

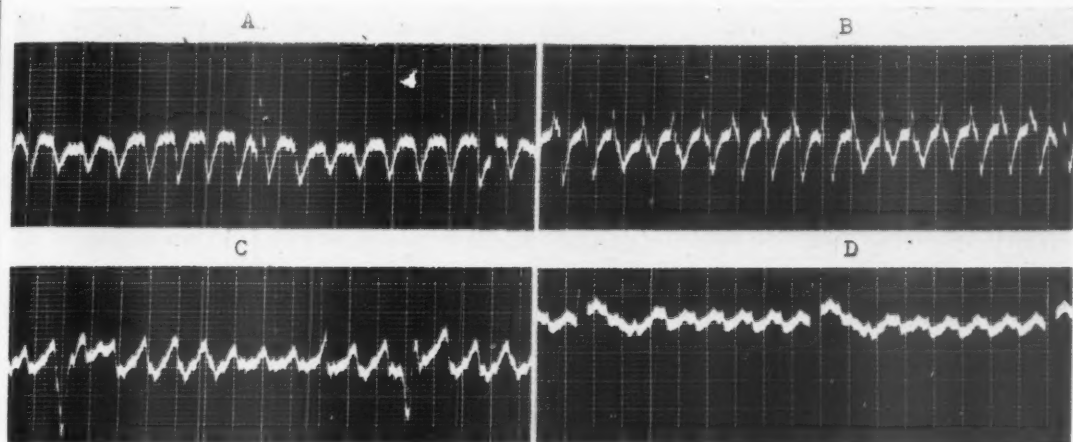


Fig. 34.—Auricular flutter. Unipolar tracings from: A, high auricular level; B, mid-auricular level; C, low auricular level; D, ventricular cavity.

At the upper auricular levels, the flutter waves were predominantly negative; at medium levels, they were diphasic and separated by a horizontal slurring which probably represents the isoelectric line; at lower levels, they were mainly positive. In tracings made from the ventricular cavity, the flutter waves were also positive but of less voltage. The ventricular complexes of this case suggest right ventricular hypertrophy.

Sinoauricular Block: Fig. 20 shows a case of sinoauricular block in a clinically normal subject.

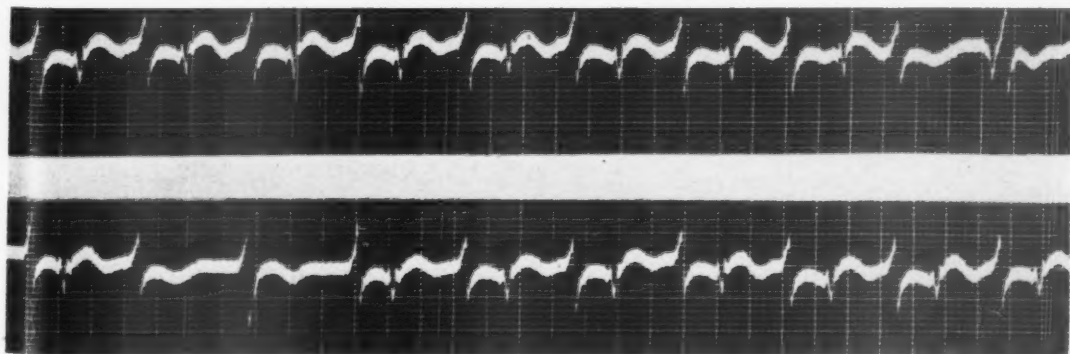


Fig. 35.—Incomplete A-V block (second degree). Continuous tracings from the mid-auricular level. Notice the auricular T wave when the A-V conduction fails.

Incomplete A-V Block: Fig. 35, a tracing made from a medium auricular level, shows this condition. The P wave is diphasic (PRs) and its voltage is greater than that of the ventricular complex. Sometimes auriculoventricular conduction fails and the auricular T wave is clearly discernible. Similar cases may be of interest for the study of auricular repolarization.

SUMMARY

The intracavity potential of the dog's heart in different experimental conditions was studied with unipolar leads. This study led to the following conclusions:

1. After ligation of the anterior descending coronary artery, the left intraventricular pattern shows depression of the RS-T segment, similar to that obtained on the posterior aspect of the heart in sites opposite to the infarcted zone. When no displacement of the RS-T segment is found, this is probably due to an incorrect placing of the electrode inside the cavity.
2. Consecutive to the ligation of the left circumflex artery the intracavity potential shows, in most of the cases, positive displacement of the RS-T segment, coincident with depression of this segment in tracings made from the epicardial surface of the injured zone. In a very few cases intracavity leads show no change while epicardial leads show a positive displacement of the RS-T segment.
3. Left and right intraventricular potentials were studied in experimental ventricular extrasystoles. When extrasystoles are initiated on the right side, the left intraventricular potential shows a diphasic QRS complex, with initial positivity of RS type; in the right intraventricular tracing, the QRS complex is always negative (QS). When ventricular extrasystoles are produced in the left ventricle, complexes of the RS type are obtained in right intraventricular leads, and complexes of QS type in leads from the left cavity. There is a very strikingly similar appearance in the pattern of intracavity potential of right ventricular extrasystoles and left bundle branch block, on the one hand, and right bundle branch block and left extrasystoles on the other.
4. After the right branch of the bundle of His was severed, intracavity potential patterns show the changes described by Wilson and associates: QS type complexes in left ventricular leads and RS type complexes in the right leads from ventricular cavity.
5. The morphology of the intracavity patterns after cutting the left branch of the bundle of His is similar to that found by Wilson and associates: QS type complex in leads from the right ventricular cavity and RS complexes in the left intraventricular tracing.
6. Complete section of the bundle of His was performed. The tracings obtained show in this case complete A-V block and idioventricular rhythm. The pattern of the intraventricular potentials is different from that found in experimental block of a single branch bundle. Ventricular complexes are never of the RS type, for they always show a slight initial negative wave.
7. After isolated section of one of the branches of the bundle of His, the QRS complex of the tracing taken inside the auricular cavity, at the side opposite

to that in which the cut was made, is similar to that found in tracings made from the homologous ventricular cavity. The tracing taken inside the auricular cavity on the same side as the block, however, does not show a ventricular complex of RS type but of qRs type.

The right intracavity potential of the human heart, in normal and pathologic conditions, was studied with unipolar leads. This study yielded the following results:

1. The normal tracing. When the electrode is located in the superior vena cava or near the sinus node, the P wave is negative (Pqs). This wave is diphasic (Prs) when the electrode is placed in the middle of the auricle. With the electrode in the lower portion of the same cavity, the diphasic P wave is predominantly positive (Prs); with the electrode in the ventricular cavity, the P wave is positive and of low voltage. The ventricular complexes taken inside the auricular cavity may have different morphology: QR, QRS, rSR' and RS. We label as "early" R the first positive deflection of the two latter types and relate it to septal activity. We designate as "late" R the positive deflection of the first two types, and the R' of the third, and relate it to the late activity of some muscular portions of the right ventricle. In tracings made from the ventricular cavity, the most frequent shape of the complex is RS. The early R is dependent upon septal activity and the S upon the activity of the free walls of both ventricles. In intracavity leads from both chambers the T wave is negative.

2. In right ventricular hypertrophy, the P wave is not modified. The ventricular complexes are of QR or qRs types. The "late" R increases in voltage and it is for this reason that we relate it to the late activity of some hypertrophied muscular portions of the right ventricle. Inside the ventricular cavity the tracing is similar to the normal one, the T wave being negative in both cavities.

3. In left ventricular hypertrophy, the P wave is not modified. The ventricular complex is similar at all auricular levels and is QS or QRS in type. The late R is absent or diminished. This is probably due to the strong vectorial forces that represent the activity of the hypertrophied free wall of the left ventricle. The ventricular tracing is always of the RS type. T is positive in both cavities.

4. In right bundle branch block the "late" R in tracings made at high auricular levels is very wide and bizarre and very similar to that seen in Lead Vr in the same type of block. The tracing is of the qR type. In tracings made at lower auricular levels the complex is qRs in type with negative T wave, much like the tracing found in the animal after cutting the branch. In the intraventricular tracing the complexes are of RS type with a negative T wave. The general form is very similar to that found in the dog.

5. In left bundle branch block the ventricular complexes obtained from inside the auricle have only negative deflections (QS) with positive T waves. In intraventricular tracings the complex of great amplitude is QS with a positive T wave. The similarity to animal tracings is striking.

6. Right ventricular premature beats have the same characteristics as those experimentally produced in animals.

7. Intracavity potential changes in certain miscellaneous conditions were studied. These conditions included subendocardial ischemia, auricular flutter, and partial A-V block.

REFERENCES

1. Wilson, F. N., Johnston, F. D., and Hill, I. G. W.: The Interpretation of the Galvanometric Curves Obtained When One Electrode is Distant From the Heart and the Other Near or in Contact With the Ventricular Surface, *AM. HEART J.* **10**:176, 1934.
2. Wilson, F. N., Rosenbaum, F. F., Johnston, F. D., and Barker, P. S.: The Electrocardiographic Diagnosis of Myocardial Infarction Complicated by Bundle Branch Block, *Arch. Inst. cardiol. México* **14**:201, 1945.
3. Sodi, P. D.: Una Interpretación a los Cambios Electrocardiográficos Consecutivos a la Ligadura de una Arteria Coronaria en el Perro, México, D. F., 1945, Libro Homenaje al Dr. Ignacio Chávez.
4. Wolferth, C. C., Bellet, S., Livesey, M. M., and Murphy, F. D.: Negative Displacement of the RS-T Segment in the Electrocardiogram and Its Relationship to Positive Displacement. An Experimental Study, *AM. HEART J.* **29**:220, 1945.
5. Lenegre, J., and Maurice, P.: Some Results of Recording Electrical Currents From the Right Auricle and Ventricle by the Direct Intracavity Lead, *Arch. d. mal. du coeur.* **38**:298, 1945.
6. Hecht, H. H.: Potential Variations of the Right Auricular and Ventricular Cavities in Man, *AM. HEART J.* **32**:39, 1946.
7. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, London, 1925, Shaw & Sons, Ltd.
8. Bayley, H. R.: On Certain Applications of Modern Electrocardiographic Theory Which Indicate Myocardial Disease, *AM. HEART J.* **26**:769, 1943.
9. Nahum, L. H., and Hoff, H. E.: The Configuration of Epicardial and Endocardial Extrasystoles in the Chest Leads, *Am. J. Physiol.* **145**:615, 1946.
10. Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., Erlanger, H., Hecht, H., Cotrim, N., Barker, P. S., Scarsi, R., and Menezes de Oliveira, R.: The Precordial Electrocardiogram, *AM. HEART J.* **27**:19, 1944.

Clinical Reports

THROMBOANGIITIS OBLITERANS IN THE NEGRO: REPORT OF A CASE AND REVIEW OF THE LITERATURE

WARREN C. BREIDENBACH, JR., M.D., AND DWIGHT M. PALMER, M.D.
COLUMBUS, OHIO

THE following case is presented as a proven instance of thromboangiitis obliterans in a Negro, an occurrence which is considered to be relatively rare.

CASE REPORT

J. E. C., a 30-year-old Negro man, was admitted to University Hospital in December, 1944, with a chief complaint of "infected toe." The immediate illness began four weeks before entry when the left great toe became "sore." A chiropodist trimmed the toenail and advised hot soaks. A week later the entire toe was fluctuant. "Numbness" became marked over the dorsal aspect of the left foot, and abnormal sweating was noticed in this area.

During the next two weeks various physicians were consulted. Many types of local treatment were attempted but the soreness progressed to a steady, severe, dull pain, present even at rest, and most severe in the calf and great toe of the left leg.

One week before admission the patient noticed that his left leg felt "cold" from toes to knee. In addition, the toes of the left leg had begun to turn "black" and appeared "withered." This, the fear of spreading infection, and the continued pain led him to seek hospital admission.

He denied pedal edema, tender subcutaneous nodules, intermittent claudication, or trauma to the legs during the four weeks prior to entry. Seven years before the present illness, however, when his job as a steel mill hooker required long hours of standing on a hot metal grill, the patient first noticed severe bilateral "arch pains" aggravated by walking, especially in cold weather, but relieved by resting during the walk. These pains recurred intermittently with exercise through five otherwise asymptomatic years. Two years before admission the patient's right great toe became "swollen and painful." Repeated visits to the outpatient department necessitated exposure to severely cold weather. Following one prolonged exposure the affected toe became "boggy" and amputation was advised and performed. No definite diagnosis was made at that time.

The past medical history was noncontributory except for the findings already mentioned. No history of syphilis was obtained. The patient had been a heavy smoker of cigarettes. The social history, obtained from the entire family, gave no evidence of intermarriage with the white race.

Physical examination showed a well-developed Negro of intelligent manner. The temperature, pulse rate, and respiratory rate were normal. The blood pressure was 140/106 in the right arm and 138/90 in the left arm. No blood pressure readings could be obtained in the legs.

From the College of Medicine, Ohio State University.
Received for publication May 23, 1946.

Examination of the left leg revealed coldness to touch from patella to toes. An area of dry gangrene of waxy purple hue involved all toes and spread in a tapering band to the lateral dorsum of the foot, where the margin of the gangrenous area was sharply demarcated, and leathery black in color (Fig. 1). The dorsalis pedis, posterior tibial, and popliteal arterial pulsations could not be felt. The femoral arterial pulsation was palpable.

Examination of the right leg revealed skin which was scaly, but of normal temperature to palpation. The great toe had been amputated. The femoral pulse was palpable, but the dorsalis pedis, posterior tibial, and popliteal pulsations could not be felt.



Fig. 1.—Area of dry gangrene with well-demarcated margin. Despite conservative therapy the area of involvement spread centrally necessitating major, though not radical, amputation. (Photograph from Dept. of Photography, Ohio State University.)

The radial, ulnar, brachial, and temporal arterial pulsations were not diminished, nor was there clinical evidence of abnormal arterial thickening.

Elevation of the feet produced minimal blanching of the plantar skin surfaces; upon dangling the feet return of apparently normal skin color was slightly prolonged.

All other physical findings were normal.

Laboratory Studies.—Quantitative dermathermic and qualitative oscillometric findings are shown in Table I. Blood studies, including a Kahn test and tests for sickleemia and for cold hemolysis were normal or negative. The glucose tolerance curve, blood uric acid, total protein and albumin-globulin ratio, cholesterol, and prothrombin level were also normal. Urinalysis, x-ray films of the chest and extremities, and examination of the cerebrospinal fluid were all negative.

Differential Diagnosis.—The history and physical examination placed the correct diagnosis in the field of peripheral vascular diseases. The patient's prolonged course, decreased arterial pulsations, and lack of systemic manifestations were sufficient grounds to rule out arterial embolism, Raynaud's disease, primary erythromelalgia, closure of an arterial aneurysm, and specific infections

TABLE I.

AREA EXAMINED	FINDINGS AFTER ONE HOUR IN CONSTANT (23° C.) ROOM TEMPERATURE	FOLLOWING SPINAL ANESTHESIA, WITHOUT USE OF VASOPRESSOR
Right knee	31.7° C. skin temperature	32.5° C. (+0.8°)
Right ankle	31.0° C. skin temperature	31.2° C. (+0.2°)
Dorsum right foot	32.0° C. skin temperature	31.6° C. (-0.6°)
Left knee	30.6° C. skin temperature	31.5° C. (+0.5°)
Left ankle	31.7° C. skin temperature	31.0° C. (-0.7°)
Dorsum left foot	30.9° C. skin temperature	30.8° C. (-0.1°)
Right popliteal space	Pulsations, low normal	No change
Right ankle	Pulsations, low normal	No change
Left popliteal space	No pulsations	No change
Left ankle	No pulsations	No change

known to cause vascular occlusions. The clinical differentiation of the more likely etiologies was very interesting.

Arteriosclerosis at the age of 30 years, limited to the legs, seemed unlikely, though "presenile arteriosclerosis" could be considered a diagnosis, or at least a terminological refuge. There was no history supporting a diagnosis of diabetic arteriosclerosis. Cold hemagglutination¹ was a possibility, since both acute episodes had started during a severe winter. In view of the patient's former occupation, the broad clinical entity termed pneumatic hammer disease² was considered. Sick cell anemia, syphilitic endarteritis, and periarteritis nodosa could not be eliminated as possibilities.

The diagnosis of thromboangiitis obliterans presented an impasse. The patient's age, the recurrent episodes of vascular occlusion, the rest pain, physical findings, and tendency towards spontaneous healing made thromboangiitis obliterans the most likely diagnosis. Only the racial axiom, still held by some, that this disease does not occur in full-blooded Negroes stood against the diagnosis.

Quantitative dermatermic and qualitative oscillometric findings were considered significant (Table I). The lack of response to spinal anesthesia was interpreted as indicating that the essential pathology was occlusive, not vasopastic, in nature.

By exclusion, the diagnosis lay between gangrene due to arteriosclerosis and gangrene due to thromboangiitis obliterans. The therapeutic implications of these two conditions are usually quite different, and the difference is of importance to a patient in the wage-earning years of life.

Both conditions deserve, and may respond to, a well-rounded course of conservative therapy. Even so, the former will more often require amputation, and at a level well above the gangrenous tissue. Thromboangiitis obliterans, however, has a somewhat more hopeful prognosis, and should amputation be necessary it is seldom justifiable to select a high amputation site.

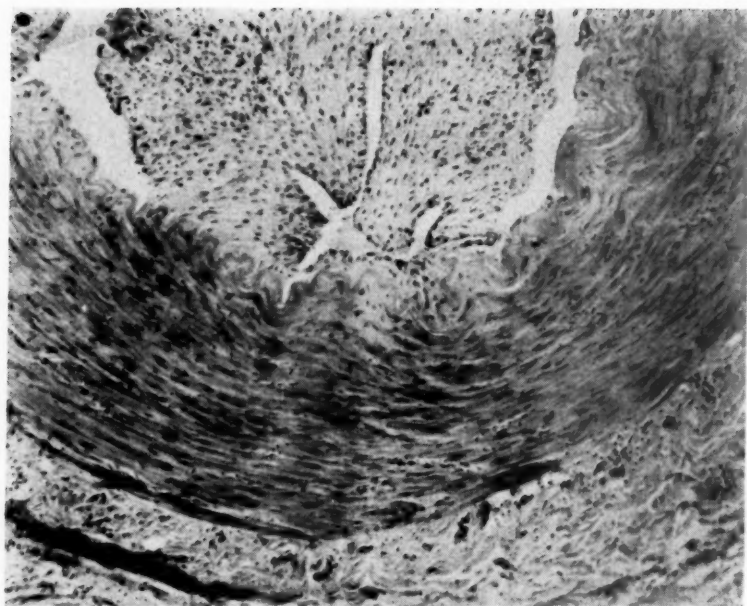


Fig. 2.—Section through the posterior tibial artery, showing a well-organized and canalized arterial thrombus occluding the vessel lumen. H. and E. stain, reduced from magnification of x175. (Photograph from Army Medical Museum, Washington, D. C.)



Fig. 3.—Section through the posterior tibial artery, showing the internal elastic lamina, seen as a wavy black line, intact. The media and adventitia are normal, and the arterial thrombus is again demonstrated. Weigert's elastic tissue stain, reduced from a magnification of x675. (Photograph from Army Medical Museum, Washington, D. C.)

Clinical Course.—On conservative therapy, including cessation of smoking, there was no improvement. The area of dry gangrene spread centrally and the severe rest pain was relieved only by continued sedation. Therefore, on the nineteenth hospital day, an amputation* was performed through the lower third of the left tibia. It was noted during the operation that the severed blood vessels showed oozing, without brisk bleeding. The course of postoperative healing was excellent.

Pathologic Findings.†—Dissection of the amputation specimen revealed, in addition to the gangrene described, some thickening and rigidity of all major arteries. This, however, was not marked; the veins appeared normal, and no matting of artery, vein, and nerve was seen.

Sections of all major vessels were taken at various levels. Microscopic sections were stained with hemotoxylin and eosin, and with Weigert's elastic tissue stain.

The major finding was a marked degree of arterial thrombosis (Fig. 2). Elastic tissue staining revealed that the intima was normal, with the internal elastic lamina intact (Fig. 3). The arterial thrombi showed advanced organization and canalization.

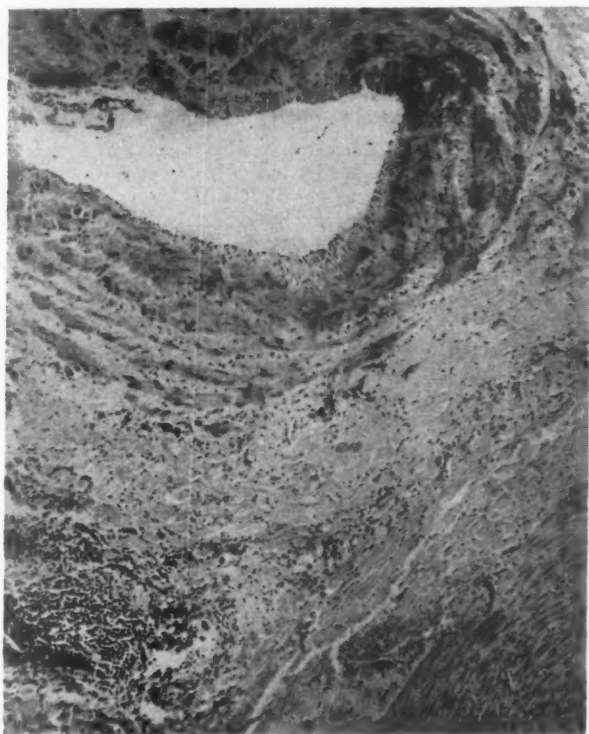


Fig. 4.—A focal collection of inflammatory cells is seen in the periadventitial connective tissue between artery below (left) and vein above. H. and E. stain, reduced from magnification of x175. (Photograph from Army Medical Museum, Washington, D. C.)

The veins did not show thromboses. There was, however, a moderate thickening of their walls. Focal infiltrations of inflammatory cells were present in the periadventitial tissues (Fig. 4). Binding of artery, vein, and nerve by fibrous tissue proliferation was not observed.

*Amputation was performed by Dr. Donald W. Traphagan of the Department of Surgery.

†Dr. Charles Chesner and Dr. H. B. Davidson of the Department of Pathology reviewed these findings and independently made a diagnosis of thromboangiitis obliterans.

DISCUSSION

Thromboangiitis obliterans is rarely seen in Negroes. Gemmil's original case³ was accompanied by an abbreviated report of the pathologic findings. A single case report⁴ by Parson did not include the pathologic findings. Smith also reported a case⁵ with an excellent history and conclusive physical findings, but lacking pathologic confirmation. Yater has presented a thorough study of five cases⁶ which included precise pathologic findings. Although every case showed clinical or serologic evidence of syphilis, one is impressed by the fact that the findings are those of thromboangiitis obliterans in all but the academic sense that in each case the disease may have been on the basis of syphilitic endarteritis. He points out, and we believe justifiably so, that there are grounds for doubt as to any connection between syphilis and peripheral vascular disease,⁷ despite the early studies of Warthin.⁸

Yater⁹ has recently described a previously unrecognized form of widespread arterial occlusion, seen in Negroes, and marked by medial fibrosis. Our case does not resemble this entity, but it is of interest to note his discussion mentioning a case of thromboangiitis obliterans in the Negro recently observed on his service.

Warshawsky,¹⁰ alone, has reported a case fulfilling the criteria of "racial purity, absence of luetic involvement, and adequate pathological evidence." We feel that it is of more than academic importance to review briefly: (1) exactly what constitutes "adequate pathological evidence" and (2) whether we are not restricting our viewpoint to the detriment of patients who will not fit a narrow category.

When Buerger¹¹ first described the three distinct phases in the pathology of thromboangiitis obliterans, he pointed out that clinical symptoms referable to vascular occlusion actually reflect the end stage in the pathologic sequence. The earlier phases, leucocytic infiltration of the veins and the formation of miliary giant cell foci, do have a clinical counterpart, namely, migrating phlebitis. When treatment is considered, however, these findings are of little moment compared to the recanalization and slow vascular occlusion seen in the final pathologic stage, repair.

The implications beyond these findings are the basis for the often stressed^{12,13,14} clinical concept: "There are few procedures more unjustifiable than radical amputation of a limb which might have sought its own level of disability."

In view of this, we do not feel that there is sufficient reason to restrict the diagnosis of thromboangiitis obliterans to those cases showing the early as well as the late phases of the pathologic sequence.

SUMMARY

A case of thromboangiitis obliterans occurring in a Negro is described. A review of all previous reports of this uncommon combination is presented. Viewpoints on what constitutes adequate pathologic evidence of this condition are considered, and treatment is discussed in relation to the sequence of pathologic changes.

REFERENCES

1. Stats, D., and Bullova, J.: Cold Hemagglutination With Symmetric Gangrene of the Tips of the Extremities: Report of a Case, *Arch. Int. Med.* **72**:506, 1943.
2. Mills, J. H.: Pneumatic Hammer Disease in Unusual Location (Posterior Tibial Thromboangiitis), *Northwest Med.* **41**:282, 1942.
3. Gemmil, W. F.: Thromboangiitis Obliterans: Report of a Case Occurring in a Negro, *Atlantic M. J.* **29**:244, 1926.
4. Parson, G. W.: Thromboangiitis Obliterans: Case in a Negroid, *Texas State J. Med.* **32**:546, 1936.
5. Smith, C. A.: Thromboangiitis Obliterans: Case in a Negro, *Texas State J. Med.* **32**:462, 1936.
6. Yater, W. M.: Thromboangiitis Obliterans in Negroes: Report of 5 Cases Studied Arteriographically and Pathologically, *AM. HEART J.* **13**:511, 1937.
7. Conner, A. A.: Development of Knowledge Concerning Role of Syphilis in Cardiovascular Disease, *J. A. M. A.* **102**:575, 1934.
8. Warthin, A. S.: Syphilis of the Medium and Smaller Arteries, *New York M. J.* **115**:69, 1922.
9. Yater, W. M.: A New Form of Generalized Arterial Disease in Negroes: Report of Two Cases, *AM. HEART J.* **30**:390, 1945.
10. Warshawsky, H.: Thromboangiitis Obliterans in the Negro: Report of a Case, *M. Bull. Vet. Admin.* **18**:83, 1941.
11. Buerger, L.: The Pathology of Thromboangiitis Obliterans, *Med. Rec.* **97**:431, 1920.
12. McKittrick, L. S.: Indications for Amputation in Progressive Arterial Obliteration of the Lower Extremities, *Ann. Surg.* **102**:342, 1935.
13. de Takats, G.: The Value of Sympathectomy in the Treatment of Thromboangiitis Obliterans, *Surg., Gynec., & Obst.* **79**:359, 1944.
14. Miller, G., and Kaufmann, M.: Thromboangiitis Obliterans: A Plea for Conservative Surgery, *Canad. M. A. J.* **19**:198, 1928.

PERFORATION OF THE INTERVENTRICULAR SEPTUM IN A CASE OF SUBACUTE BACTERIAL ENDOCARDITIS

LOUIS LEVY, II, M.D., AND EDGAR HULL, M.D.
NEW ORLEANS, LA.

PERFORATION of the interventricular septum due to subacute bacterial endocarditis is a rare condition.^{1,2} Wilson³ reported three cases of mycotic aneurysm with perforation of the interventricular septum complicating subacute bacterial endocarditis. The purpose of this paper is to present a case of subacute bacterial endocarditis complicated by perforation of the interventricular septum diagnosed during life and confirmed at post-mortem examination.

CASE REPORT

D. P., a white man, 37 years of age, entered the hospital on April 9, 1945, with complaints of fever, night sweats, and dyspnea. The patient was well until three months prior to admission, when he began to experience chills, fever, dyspnea, and palpitation. He went to see his local doctor who advised him to remain in bed; however, no specific medications were ordered. His condition grew progressively worse; his daily fever continued, he noted the appearance of some reddish spots on the palmar aspects of his finger tips, and he lost about twenty pounds during the two months prior to admission. He complained of burning of the finger tips and pain beneath the left costal margin. There was no history of symptomatology referable to rheumatic fever at any time prior to the present illness. At about the age of 17 years, during a routine physical examination, he was told that he had heart trouble. The remainder of his history was noncontributory.

Physical examination on admission revealed the following positive points: The temperature was 101°F.; pulse, 130 per minute; and blood pressure, 140/95. Numerous carious teeth were present and the gums bled on slight pressure. Murmurs interpreted as being indicative of aortic stenosis, mitral stenosis, and insufficiency were present. The spleen was palpable 4 to 5 cm. below the left costal margin, and was tender.

Laboratory work on admission revealed 4.3 million red blood cells with 76 per cent hemoglobin, a white blood cell count of 12,000 with 86 per cent polymorphonuclears, 2 per cent eosinophiles, 1 per cent monocytes, and 11 per cent lymphocytes. Sedimentation rate was 60 mm. per hour. Urinalysis on admission revealed 20 to 30 white blood cells and 40 to 50 red blood cells per high power field. Fourteen blood cultures, including four arterial blood cultures, were negative. An x-ray film of the chest showed cardiac enlargement to the left. An electrocardiogram showed R₁, R₂, and R₄ slurred, sinus tachycardia, and T₁ and T₄ inverted. Repeated agglutinations for typhoid, paratyphoid, and Brucella were negative.

A diagnosis of subacute bacterial endocarditis was based on the past history, and presence of cardiac murmurs, continued fever, evidence of emboli, and splenomegaly. The patient continued to run fever, and despite the absence of a positive culture we did not feel justified in withholding treatment. Therefore, 200,000 units of penicillin per twenty-four hours were administered daily in divided intramuscular doses every two hours for four weeks, along with hepariniza-

From the Department of Medicine, Louisiana State University School of Medicine, and the Charity Hospital of Louisiana at New Orleans.

Received for publication May 23, 1946.

tion to maintain a clotting time between 30 and 60 minutes (Lee and White) during the initial two weeks of therapy. Sulfadiazine was also employed in dosage of 1 Gm. every four hours during the entire period of treatment. He became afebrile on the fifteenth day of therapy, his febrile episodes during therapy prior to this being accounted for on the basis of heparin reactions. The patient remained afebrile after completion of therapy, and his condition improved to the point where he could be discharged three weeks later.

He was followed in the outpatient clinic, with blood cultures remaining negative. After returning home the patient remained afebrile; however, he noted a gradually increasing weakness, and fainted on exertion three times. He also complained of dyspnea on exertion, and his feet would swell in the afternoon. Since his discharge he had noted no costovertebral angle pain, petechiae, or gross hematuria. Because of his gradually increasing weakness, he was readmitted to the hospital on Nov. 1, 1945. Physical examination on his second admission revealed temperature of 98.6° F., pulse 88, blood pressure 145/69. In addition to the cardiac findings on the previous admission the following new signs were found: A systolic thrill was felt best at the left fourth intercostal space near the sternum, and a rough, loud, long, low-pitched systolic murmur was heard best over the fourth left intercostal space near the sternum, and over the lower end of the sternum. The other murmurs heard on the previous admission were still audible and unchanged from the time of discharge. The spleen had increased in size. Laboratory work showed 10 Gm. of hemoglobin and a white blood cell count of 3,900 with 65 per cent polymorphonuclear cells and 35 per cent lymphocytes. Repeated urinalyses revealed 20 to 60 red blood cells per high power field, hyaline casts, 3-plus albumin, and specific gravity varying from 1.017 to 1.014. Urea nitrogen varied from 21 to 40 mg. per cent. Repeated Fishberg concentration tests showed specific gravity varying from 1.013 to 1.016. Phenolsulfonphthalein excretion varied from 35 to 45 per cent. Nine negative blood cultures were obtained. He displayed signs of renal damage and cardiac insufficiency in the presence of negative blood cultures, and an afebrile state which we decided represented the bacteria-free stage of subacute bacterial endocarditis. The other speculation made at this time concerned the etiology of the murmur first noted on his second admission. We believed that there was an extension of the vegetation from the aortic valve on to the interventricular septum with a subsequent perforation of the septum producing a communication between the right and left ventricles, resulting in the appearance of the murmur described above. During the next few months the patient's condition grew progressively worse with renal and cardiac failure becoming prominent. About two weeks prior to the patient's death the murmur believed to be due to an interventricular septal defect disappeared.

Necropsy Report.—Permission was granted for a partial autopsy.* The heart weighed 58.3 grams. The valvular measurements were as follows: tricuspid, 12.0 cm.; mitral, 11 cm.; pulmonary, 8.0 cm.; and aortic, 10 centimeters. The wall of the left ventricle was 1.7 cm. in thickness, and that of the right ventricle, 0.4 centimeters. There was a small amount of subepicardial fat. On the anterior surface of the left ventricle, just lateral to the interventricular groove, there was seen a fibrous adhesion measuring 0.5 cm. in length. Both ventricles were dilated. The myocardium was dark red and flabby. The papillary muscles were a mottled yellow-red. The chordae tendineae of the mitral valve were thickened and shortened. The posterior valve leaflet was thickened and partially calcified, with many small nodules seen on its surface. MacCallum's area was roughened. All cusps of the aortic valve had rolled edges, with 0.1 cm. calcified nodules being most prominent along the line of closure and being disseminated throughout the aortic and ventricular surfaces of the cusps. There was an 0.8 cm. nodular elevation on the right posterior cusp. There was widening of all commissures, but the attachment was at the normal level. At the base of the right posterior cusp was an oval perforation measuring 0.4 cm. by 0.5 cm., which connected the left and right ventricles. This perforation traversed the membranous portion of the interventricular septum. The edges were smooth, round, grey, firm, and fibrous. This perforation was covered on its left ventricular aspect by a fibrinous sheath. Just to the left of this perforation, at the base of the left posterior cusp, was an additional 0.2 cm. pocket which extended into, but did not perforate, the interventricular septum (Fig. 1). The tricuspid

*Autopsy was performed by Dr. Philip Pizzolato.



Fig. 1.—Left ventricular aspect of perforation in interventricular septum.



Fig. 2.—Right ventricular aspect of perforation in interventricular septum.

valve showed a slight thickening of the cusp edges. On the right side the perforation was seen at the base of the medial leaflet of the tricuspid valve (Fig. 2). The pulmonic valve was normal except for a few firm nodules, 0.1 cm., on the ventricular surfaces of all cusps. The coronary arteries were patent throughout. A few yellow atheromatous plaques were seen in the aorta.

Microscopic sections of the mitral valves stained with hematoxylin and eosin revealed a large amount of fibrosis, some of which was completely hyalinized, and areas of chronic granulation tissue characterized by dilated, thin-walled capillaries surrounded by lymphocytes, macrophages and a few plasma cells. In these areas of fibrosis there were small irregular deposits of calcification. Extravasated red blood cells were seen in another area adjacent to the chronic granulation tissue, and numerous macrophages filled with hemosiderin pigment were present. Gram stain of the mitral valve showed no bacteria present. The aortic valve revealed a large amount of hyalinized connective tissue in which only a few pyknotic elongated nuclei were encountered. In less hyalinized places there were areas of chronic granulation tissue with fibrosis similar to those of the mitral valve. Areas of calcification, as previously described, were seen. Gram stain of the aortic valve showed no bacteria present.

Microscopic sections of the myocardium revealed myocardial fibers of the usual size. The cross striations were not prominent. Adjacent to some of the blood vessels in the connective tissue were lymphocytes and macrophages; however, no true Aschoff cells were seen. Microscopic section through the area of perforation showed a large amount of fibrosis; at the periphery chronic granulation tissue was composed of partially hyalinized capillaries surrounded by macrophages, lymphocytes, and a few plasma cells. Examination of the kidneys revealed numerous petechiae in the cortex. The line of demarcation between medulla and cortex was distinct. The cortical and medullary striations were prominent. Microscopic examination of the liver, spleen, and kidneys revealed marked congestion. The lungs showed bronchopneumonia and marked congestion.

SUMMARY AND CONCLUSIONS

A case of subacute bacterial endocarditis has been presented in which treatment with penicillin caused the establishment of a bacteria-free stage. A perforation of the interventricular septum was diagnosed during life and confirmed at post-mortem examination. This case demonstrates the need for an early diagnosis and institution of treatment with penicillin, in adequate amounts over a sufficiently long interval of time, if one is to avoid permanent renal and cardiac damage which will cause the patient's death despite the disappearance of the vegetations from the heart valves.

REFERENCES

1. White, P. D.: *Heart Disease*, ed. 3, New York, 1944, Macmillan.
2. Libman, E., and Friedberg, C. K.: *Subacute Bacterial Endocarditis*, X-A, p. 346 (1), *Oxford Medicine (Christian) VII*, part II. New York, 1940, Oxford University Press.
3. Wilson, C. P.: Mycotic Aneurysm Involving the Intraventricular Septum, *AM. HEART J.* 1:703, 1926.

DISSECTING ANEURYSM WITH HEMOPERICARDIUM

REPORT OF A CASE

GEORGE M. ELLIS, M.D.

TOLEDO, OHIO

PHYSICIANS are rapidly becoming more aware of the possibility of dissecting aneurysm in cases of sudden thoracic pain. Shennan,¹ in his comprehensive review of the literature up to 1933, accepted six cases in which a correct diagnosis had been made ante mortem. Since then, however, many cases have been diagnosed, and there have been excellent recent reviews of the subject.²

The most frequent complication of dissecting aneurysm, terminal rupture into the pericardial sac, has occurred in approximately 70 per cent of the previously reported cases. Only one other case³ was encountered in which preterminal tamponade occurred; this was immediately recognized and temporarily relieved by pericardicentesis. In the following case it seems evident that the tamponade occurred concurrently with the original dissection, as signs of cardiac compression, notably a marked pulsus paradoxus, were noted shortly after the onset of pain and persisted until death two days later. The presence of these signs greatly aided in the establishment of a clinical diagnosis.

CASE REPORT

D. R., a 67-year-old businessman, was brought to the emergency room of the Toledo Hospital at 11:10 P.M., Dec. 24, 1945. The complaint was that forty-five minutes before, while pushing his automobile, he had suddenly developed a severe retrosternal pain which was constant and did not radiate. cursory examination revealed findings not incompatible with coronary thrombosis, and electrocardiographic confirmation of this tentative diagnosis was immediately sought.

The electrocardiogram (Fig. 1) showed sinus rhythm with marked left axis deviation. There was no displacement of the RS-T segment nor other QRS or T-wave changes that could be interpreted as even suggestive of myocardial ischemia or recent infarction.

From his wife it was learned that he had had hypertension for a number of years. His blood pressure had been 156/110-100 in 1940, and 168/104 in 1941, as recorded on two previous admissions for unrelated complaints. The blood Wassermann and Kline had been negative in 1940. Otherwise the past history was essentially negative.

The physical examination revealed a well-developed and well-nourished elderly white man of hypersthenic habitus, acutely and severely ill. He was sweating profusely. Neither dyspnea nor cyanosis was evident. He was partially confused and disoriented so that it was not possible to obtain a detailed description of the nature of his pain. Temperature was 98°F. Head, eyes, ears, nose, and throat were negative. The neck was flaccid, and the jugular veins were not con-

From the Department of Medicine of the Toledo Hospital.
Received for publication May 31, 1946.

spicuous. There were fine inspiratory râles in both lung bases. Respirations were 16 per minute and neither predominately thoracic nor diaphragmatic in type. The pulse rate was 76 per minute, and the volume seemed equal in both radial arteries. Slight waxing and waning of the radial pulse related to respirations was noted. On sphygmomanometry the beats faded out on inspiration, so that the systolic pressure during that phase was approximately 37 mm. lower than

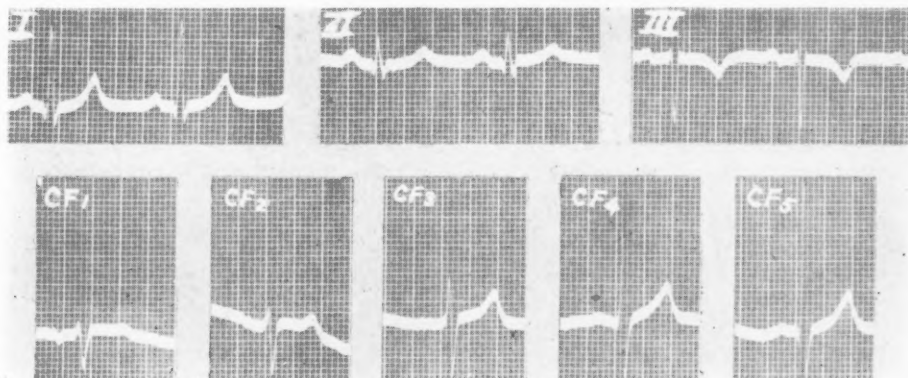


Fig. 1.—Electrocardiogram showing left axis deviation without other abnormality.



Fig. 2.—Dissecting aneurysm. Two-meter overhead film taken post mortem. There is a generalized enlargement of the cardiac shadow. The diaphragms are at a high level. The lung markings are not significant.

during expiration. The blood pressure was 165-135/95. The apical impulse was in the sixth intercostal space 5 cm. to the left of the midclavicular line. No thrills were present. The rhythm was regular. There was a blowing, grade 3, systolic murmur which was audible over the entire precordium, but most marked in the aortic area. The second sound at the base was not accentuated, and there was no diastolic murmur.

The liver edge was barely palpable beneath the costal margin, and the upper border of hepatic dullness was in the fifth intercostal space. Otherwise, the abdomen was negative. There was no edema of the extremities and no changes or inequalities in the reflexes.

A diagnosis of dissecting aneurysm of the aorta with hemopericardium was ventured at this time.

Laboratory studies showed a hemoglobin of 15.1 grams, 5,510,000 red cells, leucocytosis of 20,200 with 66 segmented polymorphonuclear leucocytes, 23 band forms, 4 mature lymphocytes, 6 monocytes, and 1 eosinophile. The erythrocyte sedimentation rate was 18 mm. per hour. A trace of albumin and a moderate number of coarse granular casts were found in the urine specimen. The nonprotein nitrogen was 60 mg. per 100 c.c. of blood on December 26.

The morning after admission the status of the patient had not changed significantly. Morphine and dilaudid had been used to control pain. The paradoxical pulse was noted again in all palpable arteries. The blood pressure was 175-150/105 in the right arm; slightly lower in the left.

The second morning after admission the temperature had risen to 102.8°F. A chest film made with a portable apparatus showed marked mediastinal widening and cardiac enlargement, but was deemed unsatisfactory for interpretation. A second electrocardiogram was similar to the first. On the evening of the second day the patient showed periorbital edema, distended jugular veins, and cyanosis. The blood pressure was 180-150/120. Cardiac and pulmonary findings were the same as on admission. Venous pressures were obtained by direct manometric method in both arms and the left leg; these were equal at 200 millimeters. A 22 gauge needle was used, and respiratory variations in venous pressure were not observed. Circulation times were attempted, but the patient was unable to give an accurate end point. It was decided to transport the patient, in bed, to the x-ray department for a more satisfactory film. In transit he had a second severe chest pain, became intensely cyanotic, and died within a few minutes, forty-five hours after his first attack. A two-meter overhead film was taken postmortem (Fig. 2).

*Autopsy.**—The positive findings were limited to the heart, aorta, and kidneys. The heart and pericardium extended to the seventh interspace on the left side and to the anterior axillary line. The right side extended slightly to the right of the right sternal line. There was considerable effusion of blood in the soft tissues of the mediastinum. The pericardial cavity contained approximately two pints of blood, largely in blood clots. The blood had apparently escaped through a tear in the adventitia of the aorta and another tear in the intima.

The heart weighed 500 grams. There was enlargement of the left ventricle. The pericardium was covered by a moderate amount of subepicardial fat which was distributed in normal depots. The left coronary artery was thickened and showed partial occlusion of the lumen due to intimal proliferation. The left ventricular wall measured 2 cm. at the base and 1.2 cm. at the apex. The right ventricular wall measured 4 mm. The left ventricular and auricular chambers were dilated. The valve leaflets showed no gross abnormalities. The circumferences of the valves were within normal limits. The mouths of the coronaries were patent. The endocardium was smooth and glistening.

The aorta was of decreased elasticity and of average width. The intima showed areas of thickening, but there was no necrosis or calcification. There was a tear of the intima halfway across the aorta, 5.6 cm. above the aortic leaflets. There was separation of the aorta extending to the renal arteries and presence of large amounts of fluid and clotted blood in the tissues. The separation was between the intima and part of the media, and between the media and adventitia. There was a tear in the adventitia with blood in the soft tissues. Sections of the aorta showed hemorrhages and patchy areas of Erdheim's medial necrosis.

The kidneys weighed 350 grams. The capsules stripped with some difficulty leaving an evenly granular surface. The cut surface showed a narrow cortex with indistinct striations. The glomeruli were gray pin points. The medulla was purple. The pelves and ureters were normal.

Cause of death: Dissecting aneurysm of aorta and hemopericardium.

*Performed by Dr. Bernhard Steinberg.



Fig. 3.—Heart and aorta. The intima with a part of the media is separated from the remaining coats, part of the media, and adventitia by fresh and clotted blood.

COMMENT

The mode of production of the signs of cardiac compression in pericardial effusion has been investigated⁴ and found to be dependent upon increase in intrapericardial pressure. In inflammation of the pericardium the normally inelastic membrane becomes dilatable, as was early commented upon by Barnard⁵ and Mackenzie.⁶ In noninflammatory pericarditis, however, a small amount of fluid suffices to increase greatly the intrapericardial tension with the production of

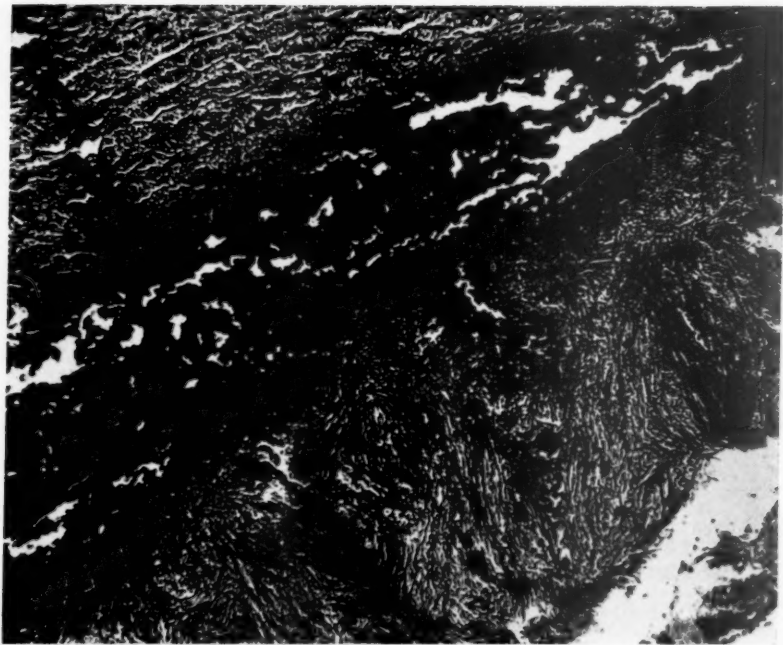


Fig. 4.—Dissecting aneurysm. Aorta $\times 100$. The diffuse black area represents blood in the media. The smaller black dots are areas of medial necrosis of Erdheim.

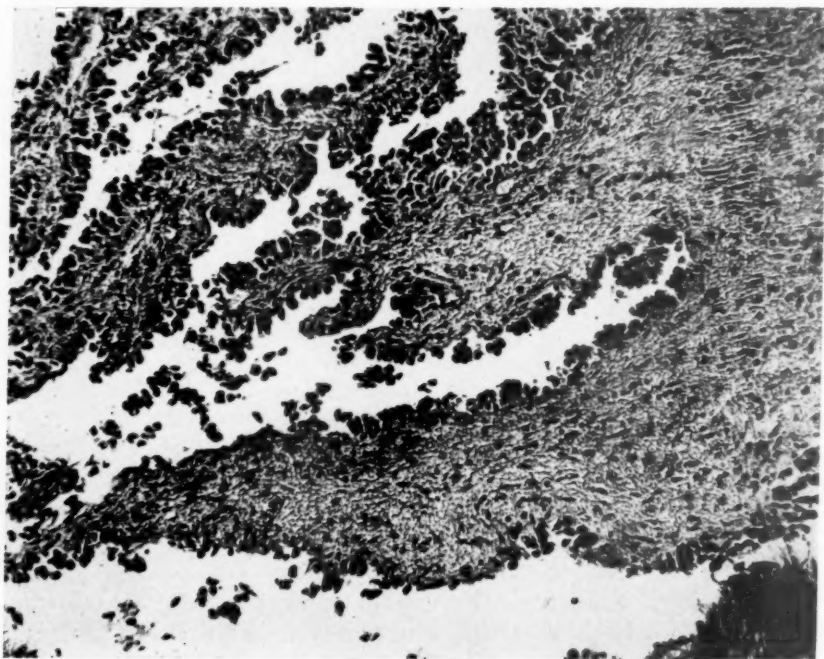


Fig. 5.—Dissecting aneurysm. Aorta. Cystic area in the wall of aorta with honeycombing effect. The cyst is lined by tall columnar epithelium.

the paradoxical pulse and other signs of cardiac embarrassment. When the height of the intrapericardial pressure equals the venous pressure, the circulation is brought to a standstill, as shown by Kuno.^{4h} From these considerations it is apparent that a sudden tamponade, as in hemopericardium from dissecting aneurysm or stab wounds,⁷ would be expected to produce a greater increase in the intrapericardial pressure than the gradual accumulation of a much larger amount of fluid in pericarditis.

In the case presented here the pulsus paradoxus, or Griesinger-Kussmaul sign,⁸ first focused attention upon the pericardium. The possibility that the respiratory variation in systolic pressure may have been produced by partial occlusion of the aortic lumen by intramural extravasation of blood without hemopericardium is quite unlikely and is not in accord with the experimental observations of Katz and Gauchat.^{4c,d}

These workers arrived at the following conclusions in their study of pulsus paradoxus: "With the pericardium distended with fluid, not only is the flow of blood into the heart impeded, but the inflow also varies during inspiration and expiration, owing to the fact that the respiratory variations of intrathoracic pressure do not affect the intrapericardial and intracardiac pressures as much as those on the entering veins. This causes a smaller difference of pressure between the veins and heart during inspiration and allows less filling of each ventricle. Consequently, a paradoxical pulse probably appears in both pulmonary and systemic circuits, but obviously the arterial pulsus paradoxus is due to the impaired inflow into the left ventricle."

SUMMARY

A case of dissecting aneurysm with hemopericardium is presented. This diagnosis was made two days before death on the basis of the history, negative electrocardiographic findings, and signs of cardiac compression, especially the pulsus paradoxus. The physiologic basis of these signs is reviewed, and the likelihood of their occurrence in hemopericardium is suggested.

Appreciation is due Dr. Steinberg, Dr. N. Worth Brown for his valuable suggestions and criticism, and Dr. Frank Clifford for his permission to report this case.

REFERENCES

1. Shennan, T.: Dissecting Aneurysms, Medical Research Council, Special Report Series, No. 193, London, His Majesty's Stationery Office, 1934.
2. (a) Holland, L. F., and Bayley, R. H.: Dissecting Aneurysm; A Report of Nineteen Cases, With a Review of the Recent American Literature, *AM. HEART J.* **20**:223, 1940.
(b) Thomas, M. E., and Garber, A. E.: Two Cases of Dissecting Aneurysm of the Aorta With Antemortem Diagnosis, *AM. HEART J.* **25**:407, 1943.
(c) Mote, C. D., and Carr, J. L.: Dissecting Aneurysm of the Aorta, *AM. HEART J.* **24**:69, 1942.
(d) Bay, E. B.: Dissecting Aneurysm of the Aorta, *M. Clin. North America* **28**:112, 1944.
(e) Logue, R. B.: Dissecting Aneurysm of the Aorta, *Am. J. M. Sc.* **206**:54, 1943.
(f) Flaxman, N.: Dissecting Aneurysm of the Aorta, *AM. HEART J.* **24**:654, 1942.
(g) Sailor, S.: Dissecting Aneurysm of the Aorta, *Arch. Path.* **33**:704, 1942.
(h) Schnitker, M. A., and Bayer, C. A.: Dissecting Aneurysm of the Aorta in Young Individuals, Particularly in Association With Pregnancy With Report of a Case, *Ann. Int. Med.* **20**:486, 1944.

3. Lawrence, J. H.: The Clinical Signs and Symptoms of Dissecting Aneurysm of the Aorta (With Report of a Case Diagnosed During Life), *Internat. Clin.* **2**:122, 1935.
4. (a) Beck, C. S.: Acute and Chronic Compression of the Heart, *AM. HEART J.* **14**:515, 1937.
(b) Beck, C. S.: Compression of the Heart, *Radiology* **37**:47, 1941.
(c) Gauchat, H. W., and Katz, L. N.: Observations on Pulsus Paradoxus (With Special Reference to Pericardial Effusions). I. Clinical, *Arch. Int. Med.* **33**:350, 1924.
(d) Katz, L. N., and Gauchat, H. W.: Observations on Pulsus Paradoxus (With Special Reference to Pericardial Effusions). II Experimental, *Arch. Int. Med.* **33**:371, 1924.
(e) Starling, E. H.: Some Points in the Pathology of Heart Disease, *Lancet* **1**:652, 1897.
(f) Cohnheim, J.: Lectures on General Pathology: A Handbook for Practitioners and Students, Section I. The Pathology of the Circulation; translated by A. B. McKee, London, New Sydenham Society **1**:26, 1889.
(g) Lewis, T.: Studies of the Relationship Between Respiration and Blood Pressure; The Effect of Changes of Intrapericardial Pressure on Aortic Pressure, *J. Physiol.* **37**:213, 1908.
(h) Kuno, Y.: The Mechanical Influence of Fluid in the Pericardium on the Function of the Heart, *J. Physiol.* **51**:221, 1917.
(i) Fineberg, M. H.: Functional Capacity of the Normal Pericardium: An Experimental Study, *AM. HEART J.* **11**:746, 1936.
(j) Stewart, H. J., Crane, N. F., and Dietrick, J. E.: Studies of the Circulation in Pericardial Effusion, *AM. HEART J.* **16**:189, 1938.
5. Barnard, H. L.: Certain Points in the Pathology of the Pericardium, *Lancet* **1**:1080, 1899.
6. Mackenzie, J.: Diseases of the Heart, ed. 3, London, 1913, Henry Frowde; Hodder and Stoughton, Ltd., Oxford University Press, p. 283.
7. Warren, J. V., Brannon, E. S., Stead, E. A., and Merrill, A. J.: Pericardial Tamponade From Stab Wound of the Heart and Pericardial Effusion or Empyema: A Study Utilizing the Method of Right Heart Catheterization, *AM. HEART J.* **31**:418, 1946.
8. Kussmaul, A.: Ueber schwierige Mediastino-Pericarditis und den Paradoxen Puls, *Berliner klin. Wchnschr.*, **10**:433, 1873.

SPONTANEOUS MEDIASTINAL EMPHYSEMA WITH ACUTE RIGHT VENTRICULAR STRAIN

ARTHUR KLEIN, M.D.
RICHMOND, VA.

SPONTANEOUS mediastinal emphysema is uncommon and still unfamiliar to many clinicians; nevertheless, reports of this condition appear in the literature more and more frequently. The occurrence of interstitial emphysema of the lungs and of mediastinal emphysema has been recognized for years. It is not rare following stab wounds or other trauma of the chest, as the result of the stresses of various respiratory diseases in childhood, and also following the use of positive pressure intratracheal anesthesia.

A case of pneumomediastinum has been observed which demonstrates what has been found experimentally but observed in no previous case: namely, the development of acute cor pulmonale during an attack of mediastinal emphysema without discernible pneumothorax.

CASE REPORT

A 16-year-old Negro boy was admitted to the hospital complaining of soreness in the neck and chest. Two days before admission, headache and malaise appeared. The day before admission he awoke with dyspnea and slight nonproductive cough. That evening he first developed pain and soreness of the chest and neck, which was aggravated by coughing and swallowing. This pain was localized over the precordium and anterior portion of the neck. There was moderate malaise but no nausea or vomiting. The patient had had uncomplicated measles and pertussis in early childhood. For several years he had suffered with bronchial asthma which improved with treatment. In the two years before admission, asthmatic attacks occurred only with upper respiratory infections.

On admission the temperature was 101.2°F., the pulse rate, 88; and respirations, 23 per minute. The blood pressure was 100/70. The patient, a well-developed, slender lad, complained of dyspnea and severe pain beneath the sternum and in the anterior neck. The pupils were equal and reacted to light and accommodation. Ophthalmoscopic examination was negative. The ears were normal. The nasal mucous membranes were congested and there was some mucoid discharge. The tonsils were enlarged and cryptic, with exudate in the crypts. The neck was held stiffly and the patient complained bitterly of pain in the anterior cervical region on flexion and extension. The cervical and submaxillary lymph nodes were slightly enlarged and firm. The chest was somewhat emphysematous and there was definite limitation of expansion of the left thorax. Percussion revealed resonance throughout, and tactile fremitus was normal. Breath

From the Department of Medicine, Medical College of Virginia and the Medical College of Virginia Hospital.

Received for publication July 22, 1946.

sounds, however, were asthmatic, with many coarse râles and rhonchi. The area of cardiac dullness was of normal size; the heart sounds were normal and no murmurs were audible. The abdomen was negative. Tendon reflexes were sluggish and Kernig's sign was absent.

Laboratory Findings.—Urinalysis was essentially normal except for rare granular casts and 2 white blood cells per high power field. The blood examinations showed 16.0 Gm. of hemoglobin, 5,640,000 erythrocytes, and 10,400 white blood cells, of which 84 per cent were polymorphonuclears, 2 per cent eosinophiles, 12 per cent lymphocytes, and 2 per cent monocytes. The sedimentation rate was 6 mm. in one hour. The blood sugar was 99 mg. per cent. The non-protein nitrogen was 27 mg. per cent. The blood Wassermann was negative. The spinal fluid showed a normal pressure, three lymphocytes, a total protein of 15 mg. per cent, and a negative Wassermann.

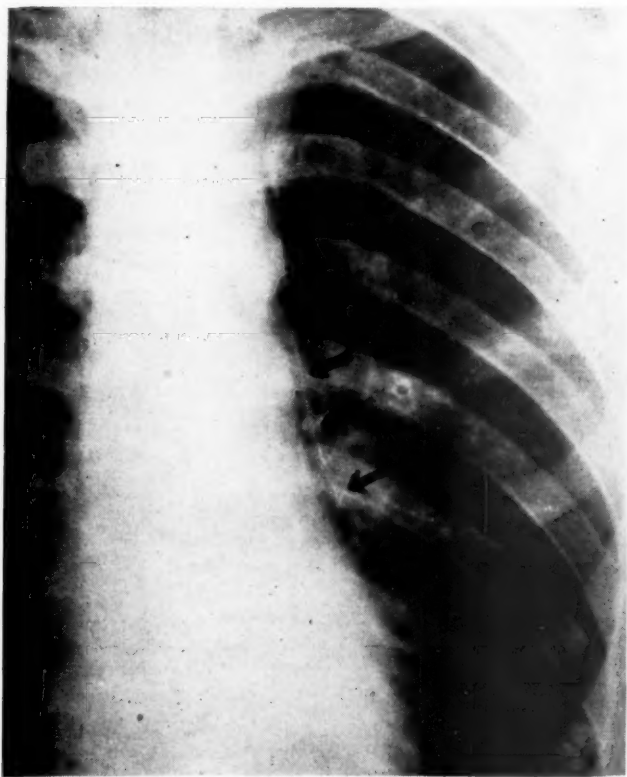


Fig. 1.—Roentgenogram of chest demonstrating air in the mediastinum.

On the day after admission, loud crackling sounds were heard over the entire precordium; the accentuation was synchronous with the heart beat. This sound resembled most closely the crunching of cellophane, and was heard to the left as far as the heart sounds were audible. The area of cardiac dullness was completely obliterated at this time. There was no subcutaneous emphysema or emphysema of the neck tissues. Pain in the substernal area and in the neck became extremely severe. Examination of the lungs revealed only suppression of breath sounds over the left chest anteriorly. By the following day symptoms were relieved slightly, although the crunching precordial sounds were still present. Within the next few days the area of cardiac dullness became percussible and the bruit over the heart disappeared entirely. All symptoms gradually cleared.

For the first three days of hospitalization the patient's temperature ranged between 99 and 101.6°F.; thereafter it was normal. The white blood cells rose to 16,200, with 91 per cent polymorphonuclear cells, and then fell to 8,550. The blood pressure ranged constantly about 110/60. The circulation time at the height of the illness was 13 seconds (arm-to-tongue with decholin); venous pressure was 120 mm. of normal saline. The sputum was negative for tubercle bacilli and the tuberculin test was negative (1:1,000).

Roentgen Examinations of Chest (Figs. 1 and 2).—Films made on the *first* day showed the chest to be emphysematous and revealed fibrosis in both lungs. The findings suggested an asthmatic type of chest with no tuberculosis or pneumonia. The heart was normal. On the *second* day a fluoroscopic examination showed the left diaphragm to be depressed and limited in motion. Air was seen in the anterior and posterior mediastinum. No pneumothorax was observed. Films on the *second* day confirmed the presence of air along the left mediastinal border and adjacent to the pericardium, both anteriorly and posteriorly. The air extended much higher than the pericardial attachment. There was no visible pneumothorax. The lungs showed increased bronchovascular markings. On the *eighth* day films showed much less air along the left border of the pericardium and mediastinum. On the *fourteenth* day fluoroscopic examination showed that both diaphragms moved well and that the heart was normal and the lungs clear though emphysematous.

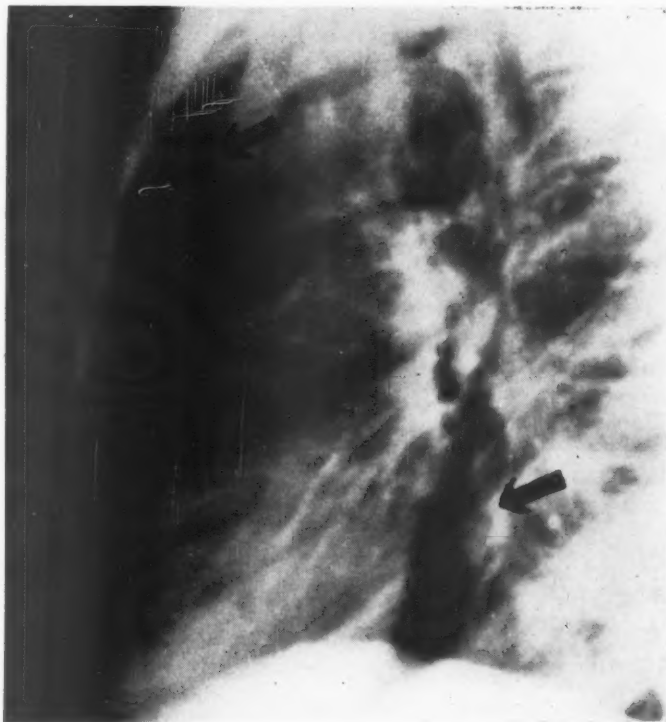


Fig. 2.—Left lateral roentgenogram also demonstrating pneumomediastinum.

Electrocardiograms (Fig. 3, A, B, and C).—Tracings made on the *third* day showed a deep S wave and a diphasic T wave in Lead I. In Lead II the P waves were peaked and the T waves of low amplitude. The findings in Lead III were peaked P waves, deep Q waves, and diphasic T waves of small amplitude. In Lead CR₄ the T waves were diphasic. These findings were interpreted to indicate right axis deviation and acute right ventricular strain. Tracings made

on the *fifth* day showed the P waves to be normal. There was a persistence of deep S waves in Lead I and Q waves in Lead III. The T waves were returning toward a normal appearance. Tracings taken on the *thirteenth* day showed the T waves to be entirely normal.

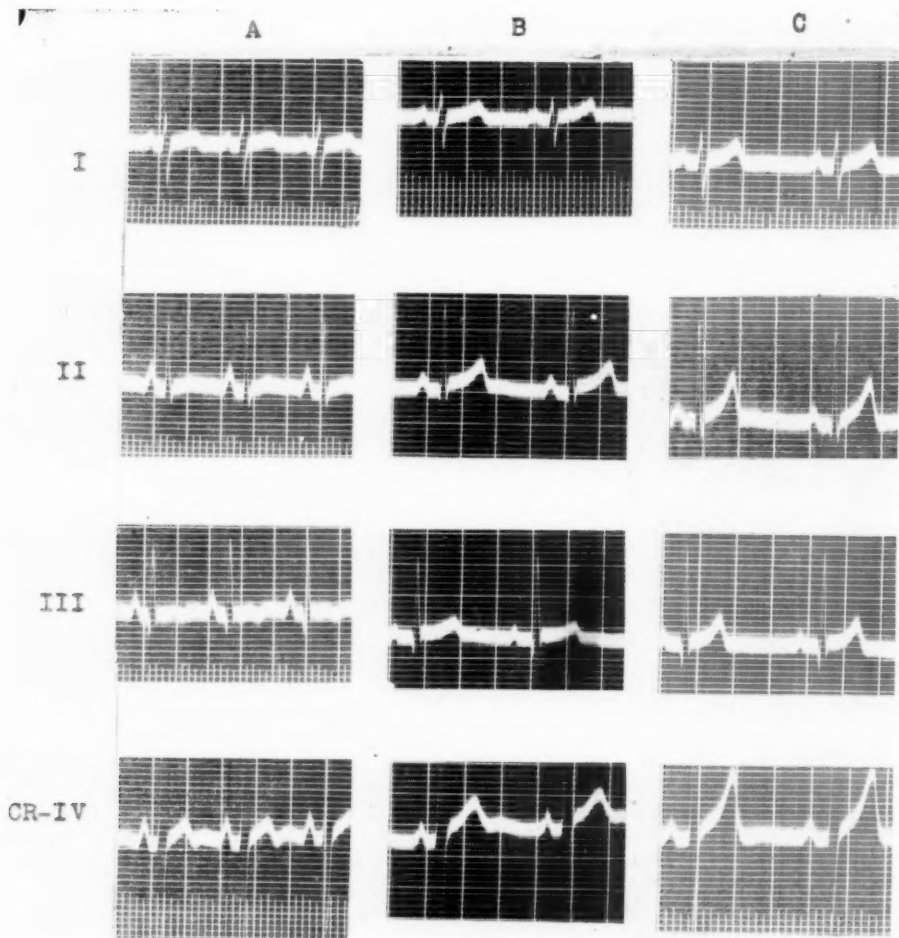


Fig. 3.—Electrocardiograms taken: A, third day; B, fifth day; and C, thirteenth day after admission.

DISCUSSION AND COMMENT

Increasing numbers of cases of spontaneous mediastinal emphysema, with or without complicating pneumothorax, are being reported in adults. Hamman¹ was the first to recognize the significance of this condition and to describe the clinical findings. In 1934, he presented two cases and has since added six others.²¹ Since its first description, further cases have been reported by Scott,² McGuire and Bean,³ Morey and Sosman,⁴ Wolff,⁵ Matthews,⁶ Pinckney,⁷ Caldwell,⁸ Styron,⁹ Griffin,¹⁰ I. Miller,¹¹ Murphy and Zeis,¹² Meek,¹³ Kellogg,¹⁴ Lintz,¹⁵ Adcock,¹⁶ Munroe and Webb,¹⁷ Greene,¹⁸ Palatucci and Knighton,¹⁹ and H. Miller.²⁰

In most of the reported cases, the clinical symptoms and signs have been similar, and have followed Hamman's original description¹ of the syndrome which has been restated in all subsequent discussions. The essential features are precordial and substernal pain of rapid or gradual onset in a basically healthy person or occasionally in one with a previous history of asthma. The appearance of the pain may be so dramatic as to simulate myocardial infarction, dissecting aneurysm, pericarditis, or mediastinitis; its distribution also may resemble these conditions. Contrary to Hamman's original statement that there are no constitutional symptoms or alterations of temperature, pulse, respiration, and leucocyte count^{21b}; a few authors have reported cases presenting aberrations of these features.^{3,15,20} In practically all the reported cases, the process was suspected because of a crunching sound heard over the precordium during systole and often during both phases of the cardiac cycle. Sometimes left-sided pneumothorax occurred; in addition, the air occasionally extended into the subcutaneous tissues of the neck. The roentgenogram often was especially helpful in establishing the diagnosis by the demonstration of air in the mediastinal tissues.

The mechanism of spontaneous mediastinal emphysema has been studied most intensively by Macklin.²² In his experiments on cats he produced interstitial emphysema of the lungs by blowing air through a catheter into a local region of the lung. This caused hyperinflation of the alveoli and leakage of air through numerous ruptures into the spaces about the minute pulmonary vessels. Macklin found that a decreasing pressure gradient developed between the alveoli and the perivascular sheaths so that air continued to pass from the former to the latter. The air then followed the path of least resistance and traveled along the vascular sheaths in blebs of increasing size toward the hilum of the lung; here it ruptured into the mediastinum, collecting in large bubbles and producing the relatively familiar clinical picture. Macklin felt that pulmonary interstitial emphysema was important clinically because these air bubbles encroached upon the space of the pulmonary vascular system, and actually interfered with the circulation through the lung. He was able to demonstrate dilatation of the right heart in cats with interstitial emphysema of the lungs and mediastinum, but the only clinical instance of actual acute right heart failure in this syndrome was reported by Fisher in 1941.²³ His patient was an infant who died three and one-half hours post partum with cyanosis and dyspnea. At autopsy air blebs were demonstrated in the mediastinum and perivascular sheaths of the pulmonary arteries which were compressed and collapsed by the bubbles. The heart showed only dilatation of the right auricle and ventricle. Marcotte and co-workers²⁴ felt that the mechanism of death after intratracheal anesthesia follows exactly the scheme first described by Macklin. H. Miller²⁰ also felt that these air bubbles in the pulmonary sheaths might actually impede the pulmonary circulation with resulting right ventricular embarrassment.

There are no reported fatalities among adults with spontaneous mediastinal emphysema. Quite possibly this is due to general failure to recognize malignant cases and also because this condition is not searched for carefully at autopsy.^{22d} Thus, the demonstration of encroachment upon the pulmonary vascular bed by

air blebs must depend at present upon the clinical and laboratory methods available, the most valuable of these being the roentgenogram and the electrocardiogram. Among the reported cases, no x-ray evidences of dilatation of the right ventricle or enlargement of the pulmonic conus have been noted, although visualization of mediastinal air is not uncommon. The typical electrocardiographic pattern of acute right ventricular strain is characterized by right axis deviation with a prominent S wave in Lead I, a depressed S-T segment in Lead II and often in Lead I, a deep Q wave and an inverted T wave in Lead III, and a diphasic or inverted T wave in Lead IV. The P waves in Leads II, III, and IV also may be large and peaked.^{25,26} These are the classical features of the electrocardiogram of acute cor pulmonale, but all need not be present; a changing tracing is important diagnostically. Although pulmonary embolism most frequently produces this pattern, any process causing rapid interference with the pulmonary arterial circulation may produce a similar electrocardiographic picture. On the basis of Macklin's experiments, spontaneous pulmonary interstitial emphysema may well be one of these factors. Electrocardiograms were reported in the cases of McGuire and Bean,³ Morey and Sosman,⁴ Caldwell,⁸ Griffin,¹⁰ I. Miller,¹¹ Kellogg,¹⁴ Munroe and Webb,¹⁷ Hoffman and co-workers,²⁷ Hamman,²¹ H. Miller,²⁰ and Palatucci and Knighton.¹⁹ In none except the latter few were there any significant abnormalities. Two weeks after the onset of symptoms the patient of Morey and Sosman showed "slight right axis deviation." Caldwell stated that "there are no pathognomonic electrocardiographic changes." Electrocardiographic interpretations were available in three of Hamman's patients: in Case 1 the electrocardiogram was normal. That of Case 4 showed low voltage in Lead I and a diphasic T₂; this patient, however, also had a small left pneumothorax. Another patient (Case 7) was a short, stocky man of 25 years. During an attack the electrocardiogram revealed a prominent S₁ and right axis deviation. No further tracings were made and Hamman did not comment on the significance of this finding in an individual whose physique would suggest that he might normally show left axis deviation. The patient of Palatucci and Knighton revealed general low voltage with no other notable abnormalities. These changes were explained on the basis of the insulating effect of air in anterior pericardial tissues. Three of H. Miller's patients revealed very definite changes of various types, but the patients had pneumothorax, and the distorting effect of this process on the electrocardiogram is well recognized.

¶ In the present case report the classical clinical picture of pneumomediastinum was associated with fever and leucocytosis. With the roentgenogram, it was possible to demonstrate a moderate accumulation of air in the anterior and posterior mediastinum. An interesting point, and one of diagnostic importance, is that with blebs of air surrounding the esophagus in the posterior mediastinum, pain on swallowing became an outstanding symptom. The sounds heard over the precordium were characteristic of those now known as Hamman's sign. Hoffman and associates²⁷ have recently made phonocardiographic records of these sounds in spontaneous emphysema of the mediastinum and have demonstrated that they are synchronous with the cardiac cycle.

The series of electrocardiograms presented in Fig. 3 show the changing pattern in the development of, and recovery from, acute right ventricular strain. It is most likely that this evidence of acute cor pulmonale is a result of encroachment upon the pulmonary arteries by air in the vascular sheaths. Here the electrocardiogram has reproduced what might be expected to occur much more frequently on the basis of Macklin's experimental work. Future cases should be studied from this viewpoint in order to determine whether the mechanism in clinical cases is similar to that of experimental pulmonary interstitial and mediastinal emphysema.

ADDENDUM

Since the completion of this paper, another article has appeared reviewing the syndrome of spontaneous mediastinal emphysema.²⁸

REFERENCES

1. Hamman, L.: Remarks on the Diagnosis of Coronary Occlusion, *Ann. Int. Med.* **8**: 417, 1934.
2. Scott, A. M.: Significance of the Anginal Syndrome in Acute Spontaneous Pneumomediastinum, *Lancet* **I**: 1327, 1937.
3. McGuire, J., and Bean, W. P.: Spontaneous Interstitial Emphysema of the Lungs, *Am. J. M. Sc.* **197**: 502, 1939.
4. Morey, J. B., and Sosman, M. C.: Spontaneous Mediastinal Emphysema, *Radiology* **32**: 19, 1939.
5. Wolff, B. P.: Spontaneous Interstitial Emphysema of the Lungs, *Ann. Int. Med.* **13**: 1250, 1940.
6. Matthews, E.: Spontaneous Mediastinal Emphysema, *New Orleans M. S. J.* **93**: 523, 1941.
7. Pinckney, M. M.: Mediastinal Emphysema and Idiopathic Spontaneous Pneumothorax, *Virginia M. Monthly* **68**: 315, 1941.
8. Caldwell, H. W.: Spontaneous Mediastinal Emphysema, *J.A.M.A.* **116**: 301, 1941.
9. Styron, C. W.: Spontaneous Mediastinal Emphysema, *New England J. Med.* **225**: 908, 1941.
10. Griffin, R. J.: Spontaneous Pneumothorax, *Kentucky M. J.* **39**: 284, 1941.
11. Miller, I.: Spontaneous Interstitial Emphysema of the Lungs, *Ohio State M. J.* **37**: 1056, 1941.
12. Murphy, J. P., and Zeis, L. B.: Spontaneous Interstitial Mediastinal Emphysema, *J. Missouri M. A.* **39**: 5, 1942.
13. Meek, E. M.: Spontaneous Mediastinal Emphysema, *South. M. J.* **35**: 990, 1942.
14. Kellogg, D. S.: Spontaneous Pneumomediastinum, *Am. J. Roentgenol.* **48**: 510, 1942.
15. Lintz, R. M.: Spontaneous Mediastinal Emphysema, *Arch. Int. Med.* **71**: 256, 1943.
16. Adcock, J. D.: Spontaneous Interstitial Emphysema of the Lung, *Arch. Int. Med.* **71**: 650, 1943.
17. Munroe, D. S., and Webb, G. A. C.: Spontaneous Mediastinal Emphysema, *Canad. M. A. J.* **48**: 232, 1943.
18. Greene, J. A.: Unusual Sounds Emanating from the Chest, *Arch. Int. Med.* **71**: 410, 1943.
19. Palatucci, O. A., and Knighton, J. E.: Spontaneous Mediastinal Emphysema, *AM. HEART J.* **31**: 364, 1946.
20. Miller, H.: Spontaneous Mediastinal Emphysema With Pneumothorax Simulating Organic Heart Disease, *Am. J. M. Sc.* **209**: 211, 1945.
21. (a) Hamman, L.: Spontaneous Interstitial Emphysema of the Lungs, *Tr. A. Am. Physicians* **52**: 311, 1937.
(b) *Ibid.*: Spontaneous Mediastinal Emphysema, *Bull. Johns Hopkins Hosp.* **64**: 1, 1939.
(c) *Ibid.*: Mediastinal Emphysema, *J.A.M.A.* **128**: 1, 1945.

22. (a) Macklin, C. C.: Pneumothorax With Massive Collapse from Experimental Local Over Inflation of the Lung Substance, *Canad. M. A. J.* **36**: 414, 1937.
- (b) Ibid.: Transport of Air Along the Sheaths of Pulmonic Blood Vessels from Alveoli to Mediastinum: Clinical Implications, *Arch. Int. Med.* **64**: 913, 1939.
- (c) Ibid.: Impediment to Circulation, Occasioned by Pulmonic Interstitial Emphysema and Pneumomediastinum, *J. Michigan M. Soc.* **39**: 756, 1940.
- (d) Macklin, M. T., and Macklin, C. C.: Malignant Interstitial Emphysema of the Lungs and Mediastinum, *Medicine* **23**: 281, 1944.
23. Fisher, J. H.: Spontaneous Pulmonic Interstitial and Mediastinal Emphysema in an Infant, *Canad. M. A. J.* **44**: 27, 1941.
24. Marcotte, R. J., Phillips, F. J., Adams, W. E., and Livingstone, H.: Differential Intra-bronchial Pressures and Mediastinal Emphysema, *J. Thoracic Surg.* **9**: 346, 1940.
25. Murnaghan, D., McGinn, S., and White, P. D.: Pulmonary Embolism With and Without Acute Cor Pulmonale, With Especial Reference to the Electrocardiogram, *AM. HEART J.* **25**: 573, 1943.
26. Currens, J., and Barnes, A. R.: The Heart in Pulmonary Embolism, *Arch. Int. Med.* **71**: 325, 1943.
27. Hoffman, A. M., Pobirs, F. W., and Merliss, R.: The Phonocardiogram in Spontaneous Interstitial Emphysema of the Mediastinum, *AM. HEART J.* **26**: 686, 1943.
28. Fagin, I. D., and Schwab, E. H.: Spontaneous Mediastinal Emphysema, *Ann. Int. Med.* **24**: 1052, 1946.

Abstracts and Reviews

Selected Abstracts

Brummer, P.: The Relation of Neurocirculatory Dystonia to Essential Hypertension, Angina Pectoris, and Peptic Ulcer. *Acta med. Scandinav.* **126**:177 (Nos. II-III), 1946.

The author correlated the level of the blood pressure in 1,206 patients manifesting varying degrees of essential hypertension with the previous occurrence of symptoms of neurocirculatory dystonia as determined from careful anamnesis. He found that 26 per cent of those under 40 years of age had had such symptoms for eight years or more in the immediate or remote past. The incidence in patients over 50 years of age was 15 per cent, a difference attributed to the effect of the late war on the younger group in addition to the necessarily less accurate history of older patients. The average incidence for all was 22 per cent.

Fifty per cent of those patients under 40 years who had systolic pressures above 140 mm. Hg. recalled neurocirculatory symptoms, and similarly, 25 per cent of patients who had present or past neurocirculatory dystonia symptoms had systolic blood pressures above 140 millimeters. In patients without evidence of neurocirculatory difficulty the incidence of such hypertension was only 13 per cent. The same relation held for the diastolic pressure levels.

On the other hand, patients over 50 who had significant systolic or diastolic hypertension, had a statistically significant lower incidence of neurocirculatory dystonia, present and past, than those without such grades of blood pressure elevation.

The incidence of neurocirculatory dystonia in 90 patients with peptic ulcer and 66 patients with definite exertional angina pectoris was 16 per cent and 18 per cent, respectively; that is, of the same order as that of the groups as a whole and presumably not greatly different from the incidence in the general population.

The author concludes that the same instability of the vasomotor system that produces neurocirculatory dystonia is, at least in part, responsible for "juvenile hypertension," whereas essential hypertension (at least in those over 50) appears unrelated. He cites the unpublished work of Rahm who examined conscripts of World War I twenty years after their induction examinations and found "in many cases" normal blood pressures in those who had had elevations at the time of the original examination. From this data and his own he suggests the inference that not all hypertension in subjects under 40 years of age is continued in later life. SAYEN.

Weiner, D., and Lange, K.: The Effects and Drawbacks in the Use of Heparin in Retarding Menstruum. *Surgery* **21**:102 (Jan.), 1947.

The value of prolonged heparinization is discussed briefly and the literature on retarding menstrua reviewed. Although the clotting times obtained after a single deposition of heparin in Pitkin's menstruum shows considerable irregularity, a satisfactory elevation can be produced for twenty-four hours with large doses in experimental animals.

In small animals, repeated subcutaneous administration of heparin in Pitkin's menstruum leads to the formation of large hematomas which not only trap the heparin and prevent adequate heparinization but frequently cause the death of the animal. These difficulties are overcome in the rat by injection into the tail.

In human beings the small size of hematomas compared to the total blood volume probably renders them less important but great care should be exercised in anemic patients. NAIDE.

Saccomanno, F., Utterback, R. A., and Klemme, R. M.: Anatomic Data Regarding the Surgical Treatment of Angina Pectoris. Ann. Surg. 125:49 (Jan.), 1947.

In dogs from which a length of spinal cord had been removed, stimulation of the isolated spinal nerves was observed to produce cardiac acceleration and a rise in systemic blood pressure when the second to the sixth thoracic spinal nerves were stimulated. No change in heart rate or blood pressure was observed when the eighth cervical or first thoracic spinal nerves were stimulated, indicating that these segments do not convey any cardiac efferent fibers.

The effect on pulse rate was most marked in the second and third thoracic nerves, the effect diminished in the fourth and fifth, and only a very slight effect was observed below the fifth thoracic nerve. The effect on systemic blood pressure was more or less constant from the second thoracic down as far as the seventh thoracic nerve.

These findings suggest a sound anatomic basis for the surgical treatment of angina pectoris. By means of surgical removal or alcohol injection of the second, third, and fourth thoracic sympathetic ganglions on the affected side only, a complete alleviation of anginal pain and a reduction of coronary vasospasm should result. This single surgical procedure does not completely interrupt the pathways of sympathetic effector impulses to the head and upper extremity, since the first thoracic segment which conveys fibers to these areas, but which does not convey cardiac afferent or efferent fibers, remains intact.

NAIDE.

Tanna, J. F.: Scalenotomy. An Analysis of Eleven Cases Done for Scalenus Anticus Syndrome. Ann. Surg. 125:80 (Jan.), 1947.

The scalenus anticus syndrome is discussed, and eleven cases presenting symptoms of this entity are reviewed. Seven cases were not associated with a cervical or abnormal rib, indicating that the scalenus anticus syndrome occurs with much greater frequency than the cervical rib syndrome.

The symptoms are the result of spasm of the scalenus anticus muscle, resulting in compression of the brachial plexus and subclavian artery, with the creation of a vicious circle. Attention is called to the fact that many cases of scalenus anticus syndrome may, in reality, be secondary to some other underlying primary pathology.

Scalenotomy may not be necessary in mild cases, since conservative handling is all that is necessary to bring about permanent relief. The results following scalenotomy in the series reported were excellent, only one case of bilateral cervical ribs failed to respond to treatment.

NAIDE.

Miller, H. I., and Miller, P. R.: Refrigeration in Surgery. Am. J. Surg. 72:694 (Nov.), 1946.

The question whether refrigeration prolongs the survival time of anemic tissue remains unanswered. The evidence tends to show that it does. The blessing is not unmixed because of the fibrous replacement of nerve and muscle tissue.

The bacteriostatic action of cold in vivo is on a weak footing. In all the experimental studies cold proved to be of no value. Clinically, it was of value. O'Neil's demonstration of the value of cold in a palmar infection in a patient with scleroderma and in a patient with gas gangrene, and the appearance after refrigeration of gas gangrene in the stumps of two refrigerated limbs, merely outlines the ramifications of the problem.

The published case histories praise the value of cold in shock. Blalock's studies tend to confirm this although his results are not conclusive.

In the elderly toxic patient with gangrene and sepsis, amputation with a tourniquet and refrigeration gives excellent results. Here lies the chief indication for refrigeration amputation. Pain and shock are eliminated and the operation is performed in a bloodless field.

NAIDE.

Leitner, St. J.: Electrocardiographic and Spirometric Findings in Boeck's Sarcoid. *Cardiologia* 10:379, 1946.

Myocardial damage is common in Boeck's sarcoid and may be primary or secondary. The latter may result from active lesions or scars, the miliary pulmonary form being less damaging than an extensive sclerotic process. Seventeen patients with this disease were examined. Electrocardiograms were taken at rest, after exercise, after oxygen inhalation, and after gynergen. Oxygen was given to differentiate between organic heart disease and deficient arterialization; gynergen was given to reverse functional electrocardiographic changes. With the patients at rest, there was evidence of myocardial damage in eight patients, probable damage in two, and normal findings in seven. One had congenital heart disease. The electrocardiographic findings were prolonged A-V conduction in five patients, prolonged QRS in two, depressed T waves in five, depressed S-T segments in two, shortened Q-T interval (with hypercalcemia) in four, and supra-ventricular extrasystoles which disappeared after exercise in two patients. After exercise electrocardiographic changes became more abnormal in seven patients, but in one a prolonged P-R interval disappeared. Oxygen inhalation normalized the electrocardiograms of two patients. Gynergen normalized the tracing of one patient and made the tracing of another worse. Of the two patients with evidence of probable damage, the electrocardiogram of one became normal after exercise and one became worse. The authors recognize three possible causes for the electrocardiographic changes: infectious-toxic myocardial damage, right heart strain, and myocardial involvement by the sarcoid. The authors feel that the first is the most common and likely cause.

Spirometric examinations determined the vital capacity, reserve and complemental air, rest minute volume, and respiratory range. In eight patients the spirometric values corresponded with the clinicoradiologic findings. In others the findings did not agree or they showed little change after 3 to 12 months in spite of clinical improvement or deterioration. In general, patients with hilar involvement have better function than those with extensive pulmonary involvement. The results give valuable aid in prognosis. LENEL

Forster, Rudolf: Myocardial Damage in Starvation. *Cardiologia* 10:369, 1946.

Cardiovascular changes were found in all of fifty cases of starvation from German concentration camps. Clinical signs and cardiac failure were rare; changes were found only by electrocardiographic examination. Thirty-one noninfectious patients of all age groups were studied. All had varying grades of edema, cachexia, anemia, hypoproteinemia, and hypocholesterolemia. Fourteen patients showed a relatively low voltage which became higher after therapy. Six had absolute low voltage; two of these patients had tuberculous pericarditis. A relationship of the voltage to the amount and extent of edema was noticed. That edema is not the only mechanism responsible for the low voltage was emphasized by patients with normal voltage in spite of edema or increasing voltage in spite of the persistence of edema. Myocardial damage or hidden pericarditis in the many cases with tuberculosis was thought to be a cause.

Low T waves were found in twenty-nine patients. This change was more conspicuous than low voltage and was found in patients with normal voltage. Inverted or diphasic T waves were found only in patients in whom infectious disease or cardiac disease existed. The S-T segments, and the intraventricular and A-V conduction times were normal. The Q-T interval was prolonged in two moribund patients with diarrhea.

The author concludes that only low voltage and flat T waves are characteristic of inanition and that these changes are both reversible. This was shown by the return of a normal electrocardiogram after therapy.

Clinical examination gave no constant findings: the systolic blood pressure was usually below 100 millimeters, hemic murmurs were absent in spite of anemia, the hearts were normal or small in size, and congestion of the liver was found only on autopsy in a few cases. The edema was not influenced by cardiotonic drugs.

Eighteen patients died of complicating infections. The hearts showed brown atrophy, fatty degeneration, occasionally focal fibrosis, and cloudy swelling.

With regard to the pathogenesis, no constant relation to metabolic changes could be demonstrated. The change of the pH of the blood toward alkalinity is considered important. B₁ avitaminosis, even in the absence of a typical clinical picture, may be a factor. The sum of these changes lead to alterations of the myocardial cellular metabolism which are reversible. They also explain the rapid decline in patients with previous myocardial damage. LENEL.

Merrill, A. J., Morrison, J. L., and Brannon, E. S.: Concentration of Renin in Renal Venous Blood in Patients With Chronic Heart Failure. *Am. J. Med.* 1:468 (Nov.), 1946.

Renal venous blood was obtained through a radiopaque catheter, which had been introduced into an antecubital vein and threaded through the venous system under fluoroscopic guidance into a renal vein. The plasma was separated by centrifugation and, after special preparation, assayed for renin content by injecting it intravenously into anesthetized dogs. Dogs were used because of their relative insensitivity to renin so that a positive result would assure the presence of a significant quantity in the tested material.

Eight of eleven patients with chronic congestive heart failure had significant amounts of renin in their renal venous blood. No renin was demonstrated by this method in arterial blood from these same patients nor in arterial and renal venous blood from five normal subjects.

The authors comment upon the coexistence of the increased concentration of renin in renal venous blood and the vasoconstriction that is present in chronic congestive heart failure. This vasoconstriction maintains arterial pressure despite a reduced cardiac output. Furthermore, renal blood flow is decreased out of proportion to the fall in cardiac output. It is suggested that renin may contribute to these vasoconstrictor phenomena in chronic congestive heart failure. FRIEDLAND.

Silfverskiöld, B. P.: The Effect of Hemorrhage and Shock on the Caliber of the Abdominal Vena Cava. *Acta physiol. Scandinav.* 12:130 (Nos. 2-3), 1946.

Direct observation of the inferior vena cava in anesthetized rabbits was combined with measurement of pressure through a catheter passed into the lumen by way of the jugular vein. The caliber of the inferior vena cava became smaller when hemorrhage or shock was produced in the rabbits. The average diminution in diameter was from an initial 8 or 9 mm. to 4 or 5 millimeters.

Active constriction of the vein wall and not passive adaptation to a smaller blood content was believed to be the cause of the diminution in size, because (1) the pressure fall within the vena cava was negligible; (2) raising the caval pressure for short periods (thirty seconds) by infusing saline solution into a femoral vein or compressing the liver did not increase the caliber; and (3) tapping the vein with a finger caused a quick return to the original diameter, but the intraluminal pressure was unaltered. Since clamping the carotid arteries in other rabbits was not followed by vena caval constriction the possibility of a carotid sinus reflex as the underlying physiologic mechanism was apparently ruled out. SAYEN.

Howorth, S., McMichael, J., and Sharpey-Schafer, E. P.: Effects of Venesection in Low Output Heart Failure. *Clin. Sc.* 6:41 (Nos. 1-2), 1946.

The authors studied and compared the effects of venesection and the intravenous administration of 1.5 mg. of digoxin on blood pressure, right auricular pressure, cardiac output, and peripheral resistance in twenty-five patients with "low output" congestive heart failure which was ischemic, valvular, or hypertensive in origin. Both procedures reduced right auricular pressure: venesection transiently, and digoxin often for an "indefinite period." Cardiac output rose significantly whether there was sinus rhythm or auricular fibrillation. In almost all venesected cases the blood pressure fell considerably, and from this fact, a marked decrease in peripheral resistance (site under investigation) was inferred. The blood pressure did not fall, and often rose, after digoxin.

The rise of cardiac output after right auricular pressure was lowered was attributed to the heart's stroke volume lying on the falling, or "overloaded," portion of Starling's ventricular filling curve. Whether digoxin exerted an effect on cardiac contraction in addition to the improved efficiency resulting from lowered auricular pressure could not be determined from the data because the blood pressure fell after venesection. Whereas the heart was doing more work after digoxin, it could not be ascertained if the increased output following venesection would have been maintained under conditions that prevented a decrease of peripheral resistance. SAYEN.

Christensen, B. C.: Variations of the CO₂ Tension in Arterial Blood and the Electrocardiogram in Man. *Acta physiol. Scandinav.* 12:389 (No. 4), 1946.

The author's previous qualitative studies of the effects on the electrocardiogram of hyperventilation, he believes, have proved that the abnormal tracings are not the result of impeded dissociation of oxyhemoglobin, nor of tachycardia; that they occur despite nitroglycerin administration; and that changes in arterial pressure do not accompany them. The calcium ion content does not decrease during hyperventilation tetany, nor does the duration of electrical systole increase, as is sometimes the case in coronary insufficiency. Alteration of intramyocardial pressure with diminished coronary flow due to change in the character of systole and diastole may be the important mechanism involved.

The present study consisted of more quantitative measurements, in two normal subjects aged 30 and 42 years, of alveolar CO₂ tension during the course of hyperventilation experiments. The distinctive electrocardiographic abnormalities, consisting of RST segment depression and T-wave flattening or inversion in two or more leads, began to appear when the alveolar CO₂ tension had fallen from the normal range of 36 to 39 mm. Hg to about 20 millimeters. The changes became greater at pressures of 16 to 17 mm. Hg. They could be abolished or prevented by breathing 2 to 3 per cent CO₂ mixtures.

Since untrained or neurasthenic persons who exercise frequently overventilate, the author thinks that the hypoxemia test is more dependable in the diagnosis of coronary insufficiency than exertion tests. The low oxygen mixture, however, should contain 2 to 3 per cent CO₂ to eliminate the effects of acapnia on the electrocardiogram. SAYEN.

Holmgren, B., and Silfverskiöld, B. P.: The Volume Variations of the Large Central Blood Vessels. *Acta physiol. Scandinav.* 12:134 (Nos. 2-3), 1946.

An important blood reservoir function is ascribed to the heart, aorta, and the great vessels of the thorax. Previous studies are said to have shown that 30 per cent of the blood volume in mice and 26 per cent in rabbits is contained in these structures. The present investigation consisted of thorotrast visualization of these portions of the cardiovascular system of rabbits before and after they were subjected to a severe hemorrhage. After hemorrhage, the heart size and aortic caliber diminished greatly and this appeared to be proportionate to the fall of the systemic blood pressure. Then, somewhat later, the size of the venae cavae decreased without significant internal pressure change. The skin vessel caliber appeared to be unchanged in hemorrhage severe enough to produce the above effects. However, if ether anesthesia was pushed to the point of intoxication in other rabbits, the skin vessels became markedly constricted, whereas little change in the venae cavae was observed.

It is felt that the venae cavae calibers can vary independently of other veins and that this is due to active vasoconstriction rather than passive adaptation to a lower intraluminal pressure, as was apparently the case with the alterations in aortic size. SAYEN.

Massie, E., and Valle, A. R.: Cardiac Arrhythmias Complicating Total Pneumonec-tomy. *Ann. Int. Med.* 26:231 (Feb.), 1947.

In an analysis of a series of 120 patients undergoing total lung resection, eleven, or 9.1 per cent, were found to have developed a detectable arrhythmia sufficient to endanger the outcome of the operation or at least to cause symptomatic difficulty. The arrhythmias included five instances of auricular fibrillation, four of auricular flutter, and one each of frequent auricular and ventricular

extrasystoles. The right lung was removed in six of the patients developing postoperative arrhythmias and the left in five. The type or location of the lesion had no specific relation to the occurrence of the arrhythmia, although abnormal cardiac rhythms did develop in two of the three patients with involvement of more than one lobe. All the patients developing arrhythmias were 35 years of age or older, the greatest incidence being between the ages of 40 and 70 years. A study of the extent of the anemia before and after the operation and the number of transfusions given the individual patients revealed that these factors had no influence on the development of the cardiac abnormalities. No correlation was detected between febrile reactions and the cardiac disturbances encountered in this study. Medication given prior to the development of the cardiac difficulties also presented no etiological clue.

All the arrhythmias developed within one week after operation, one instance occurred on the second postoperative day, six on the third, two on the fourth, and one each on the sixth and seventh postoperative days. Three of the patients with cardiac arrhythmias died, and an extensive pericarditis was found in two subjects at post-mortem examination.

Twenty-six of the total group of 120 patients presented some evidence of heart involvement prior to operation either on physical or electrocardiographic examination. It is interesting to point out that only in one of these twenty-six cases was a detectable postoperative arrhythmia encountered. The arrhythmias in the remainder appeared in patients with presumably adequately functioning hearts preoperatively. Further study revealed that in addition to the eleven patients who developed abnormal cardiac rhythms, and symptoms therefrom, at least six other individuals showed some objective physical or electrocardiographic evidence of difficulty not present preoperatively.

The authors suggest that the combination of vagal irritation and anoxemia incident to the operation may be responsible for the initiation of the abnormal cardiac rhythms. It is recommended further that the patient's cardiac rhythm must be carefully and frequently observed during at least the first postoperative week in order to determine at the earliest possible moment the onset of abnormal heart action and thus permit early decision as to the therapeutic procedure of choice.

WENDKOS.

Wilhelm, F., Hirsh, H. L., Hussey, H. H., and Dowling, H. F.: The Treatment of Acute Bacterial Endocarditis With Penicillin. Ann. Int. Med. 26:221 (Feb.), 1947.

Eight patients with acute endocarditis were treated with penicillin. In every instance, two or three positive blood cultures had been obtained before treatment was begun. The causative organisms were *Staphylococcus aureus* in two cases, *Staphylococcus albus* in five cases, and a pneumococcus in one case. Five of the patients with staphylococcal infection were heroin addicts who used unsterile syringes for injecting the drug intravenously; and of this number, two were suffering from a complicating malarial infection which had been acquired by the same means.

The initial dose for all eight patients varied between 5,000 and 30,000 units every two to three hours intramuscularly or 200,000 units per day by continuous intramuscular injection. In several patients this dose had to be increased and the largest dose given was 2,000,000 units daily by continuous intramuscular infusion. The duration of treatment did not exceed eight weeks in any instance. Of the eight patients treated, three with staphylococcal endocarditis died before two days of treatment had been completed. A fourth case died because of inadequate dosage. A fifth case died of acute left ventricular failure following severe exertion at a time when the infection had apparently been brought under control by penicillin. Of the three cases who recovered, one had a *Staphylococcus aureus* infection and the other two a *Staphylococcus albus* infection. The case of *Staphylococcus aureus* infection which recovered following the use of penicillin, developed, a year later, another *Staphylococcus aureus* bacteremia. This recurrent infection was unaffected by penicillin, but responded favorably to streptomycin. It is the opinion of the authors that in the five patients who died, treatment was either inadequate or had been started too late.

WENDKOS.

Grollman, A.: Experimental Hypertension in the Dog. *Am. J. Physiol.* 147:647 (Dec.), 1946.

Experimental evidence was obtained in dogs that the hypertension resulting from renal artery constriction has at least two different factors in its pathogenesis. One, which acts immediately, is apparently identical with the generally accepted renal pressor mechanism; it is, however, unrelated to the chronic sustained rise in blood pressure which follows. Even removal of one kidney, the other remaining intact, results in a definite elevation in blood pressure. Removal of a constricted kidney does not abolish chronic hypertension which is maintained for some hours even in the absence of all renal tissue. The bearing of these experiments on hypertension in man is briefly discussed.

KETV.

Page, E. W., Ogden, E., and Anderson, E.: The Influence of Steroids on the Restoration of Hypertension in Hypophysectomized Rats. *Am. J. Physiol.* 147:471 (Nov.), 1946.

Following the establishment of experimental renal hypertension in rats, hypophysectomy or adrenalectomy causes a fall of blood pressure which may in some cases reach levels below normal. The hypertension may then be partially restored by the administration of desoxycorticosterone or adrenal cortical extracts.

KETV.

Richards, O. W., Jr.: Observations on the Dynamics of the Systemic Circulation in Man. *Bull. New York Acad. Med.* 22:630 (Dec.), 1946.

This is a concise review of recent findings by different investigators. The Fick principle and the technique of right heart catheterization are discussed, and the problem of measurement of total peripheral resistance is reviewed. Tables are included showing values for many circulatory functions at rest, during exercise, in hypertension before and after sympathectomy, after administration of a pressor drug, and in various types of shock. The review is well illustrated with pressure tracings from right auricle, right ventricle, aorta, and femoral artery under different conditions.

KETV.

Ensor, C.: The Electrocardiogram of Rats on Vitamin E Deficiency. *Am. J. Physiol.* 147:477 (Nov.), 1946.

The electrocardiogram of rats maintained for one year on a vitamin E deficient diet does not differ from that of normal rats except that a slight widening of the QRS complex occurred infrequently.

KETV.

Rivero Carvallo, J. M.: A New Sign of Tricuspid Insufficiency. *Arch. Inst. cardiol. México* 16:531 (Dec.), 1946.

The author describes a new sign which was demonstrated in 90 per cent of cases with tricuspid insufficiency.

The sign consists of the appearance and intensification of the systolic murmur over the tricuspid area, or the appearance of such a murmur when a murmur was not originally apparent, during deep inspiration or inspiratory apnea. The short inspiratory apnea of crying children may be sufficient to bring out the sign. The sign is attributed to the increased venous return associated with deep inspiration.

LUISADA.

Frau, G.: The Esophageal Lead in the Study of the Auricular Complex. *Folia Cardiol.* (Milan) 5:173 (April 30), 1946.

The author studied the auricular complex by means of a unipolar esophageal electrode. The indifferent electrode was placed on the left leg.

The auricular complex of the normal heart consists of a rapid oscillation (P_{ES}) and a slow terminal wave (T_A).

In most cases of heart disease, the esophageal lead reveals changes of the auricular complex which are not apparent in the classic leads. One case of auricular infarction was revealed by the inverted and cove-shaped T_A . The author advocates systematic use of the esophageal lead in the study of auricular activity.

LUISADA.

Deibert, A. V., and Bruyere, M. C.: Untreated Syphilis in the Male Negro: III. Evidence of Cardiovascular Abnormalities and Other Forms of Morbidity. *J. Ven. Dis. Inform.* 27:301 (Dec.), 1946.

This study is an attempt to follow the natural history of syphilis, uninfluenced by treatment, in adult Negro men, with special reference to its effect on the cardiovascular system. It was found that among untreated syphilitics and presumably unaffected controls, the proportion presenting some evidence of morbid processes of any etiology was considerably higher in the former group: 84 per cent in the syphilitic group and 39 per cent in the unaffected group. The discovered abnormal findings were most frequently associated with the cardiovascular system. The total number of recorded examinations was 423, of which 155 were untreated syphilitics, 115 were infected but had received some treatment, and 153 were believed to be nonsyphilitic. The results of this analysis indicated that the death rate among the syphilitics was more than 75 per cent greater than among the controls, and the life expectancy approximately 20 per cent less. These percentage differences were greatest in the lower age groups.

Dilatation of the ascending portion of the aorta as observed by roentgen study was shown to be more frequent in syphilitics of all ages than in controls. Definite abnormality of the aorta was observed in about 40 per cent of the syphilitics above the age of 65, while it was present in only 10 per cent of the controls. The heart size, as determined by the ratio of the transverse diameter of the heart to the internal diameter of the thorax, indicated more abnormality in the syphilitic group. The systolic and diastolic blood pressures, as well as the pulse pressures, were higher in syphilitics than in nonsyphilitics. Examination of the radial, brachial, and temporal vessels revealed evidence of arteriosclerosis more frequently in the syphilitic than in the control group. In the younger age group, the percentage of the syphilitics in whom evidences of arteriosclerosis could be detected was significantly greater than in the controls.

BELLET.

Moritz, A. R., and Zamcheck, Norman: Sudden and Unexpected Deaths of Young Soldiers. *Arch. Path.* 42:459 (Nov.), 1946.

The authors, in reviewing more than 40,000 autopsy protocols received at the Army Institute of Pathology between January 1942 and January 1946, collected approximately 1,000 cases of sudden death from disease in apparently healthy soldiers under the age of 40 years. An examination of between 700 and 800 of the protocols shows that three principal categories included the majority of these cases.

Organic heart disease accounted for approximately 250 of these unexpected deaths. Of this number, more than 200 were due to coronary arteriosclerosis, and 34 to other forms of cardiac disease. Of the coronary cases, 115 were selected for statistical study. With increasing age there was rapid rise in incidence, even in this group composed of young men. Negroes were definitely less susceptible than white persons to sudden "coronary" death. The authors did not find obesity to be a significant factor. Their data, in reference to the degree of exertion associated with sudden death from coronary disease, "do not prove or disprove a cause and effect relationship between physical activity and acute heart failure." Their analysis of ninety-eight coronary cases showed that thirty-three died in sleep, seventeen died during "strenuous exercise," and the remainder died while in a state of inactivity, or during the course of ordinary activity. The authors concur in the general opinion that violent exercise is probably dangerous for persons suffering from severe coronary disease. In all instances, severe atherosclerosis in one or both coronary arteries was disclosed by post mortem examination. Complete occlusion was absent in 55 per cent of the group, and bleeding into an atheromatous plaque was infrequent. In the large majority of cases the heart was within normal weight limits.

In the group of thirty-four cases of sudden death from cardiac disease other than coronary arteriosclerosis, there were fourteen instances of "idiopathic" acute myocarditis, five of extensive diffuse (chronic) myocarditis, six cases of syphilitic aortitis, and five cases of rheumatic heart disease.

The second great category was nontraumatic intracranial hemorrhage. This group consisted of ninety-one cases of which sixty-nine died of subarachnoid hemorrhage from congenital "berry" or "miliary" aneurysms. In this group whites predominated heavily over Negroes. Body weight seemed to be of little or no significance. There was no instance of direct cranial trauma, but strenuous physical activity was an important predisposing factor. This group of cases was arbitrarily limited to cases that did not survive more than twenty-four hours. In the majority of cases the fatal seizure was preceded by headache and vomiting, and in many cases by fecal and urinary incontinence. In this group of sixty-nine cases there were three in which there was clinical proof of blood leakage before the fatal rupture; lumbar puncture disclosed bloody spinal fluid twelve days, two months, and six months before the occurrence of the fatal hemorrhage. When these soldiers had their fatal attack they were thought to have made a complete recovery from their previous involvement.

In sixteen other cases, although spinal fluid examination was not done, there was clinical evidence of cerebral disturbance which was present from a few days to many months before the fatal attack. Severe headaches, nausea, attacks of stiff neck, malaise, and evanescent nerve palsies were noted in this group. Necropsy later revealed that the latter sign was the result of an adherent aneurysm with burrowing hemorrhage. It was apparent that when blood was extravasated into the adjacent brain substance through rupture of a superficial aneurysm it was less likely to be fatal than when blood escaped directly into the subarachnoid space. The burrowing hemorrhage therefore was considered evidence of previous involvement, and of organic fixation of the aneurysm to the adjacent brain surface.

In eighteen of the ninety-one cases of unexpected death due to intracranial hemorrhage, the origin of the bleeding was an intracerebral vessel, in contrast to the subarachnoid location of the congenital aneurysms. In five of these "internal brain hemorrhages" an aneurysm was the cause, the aneurysm in all five cases occurring in one or another branch of the middle cerebral artery. In every instance the hemorrhage had ruptured into a lateral ventricle. There were four cases of primary subarachnoid hemorrhage due to a lesion other than congenital aneurysm, namely angioma. It is interesting that there were thirteen instances of intracerebral bleeding in which neither the exact site or nature of the vascular defect could be recognized. In all of these cases the hemorrhage originated in the lenticulostriate region. The soldiers who developed this condition were never previously ill and necropsy did not reveal any evidence, other than the hemorrhage, of cerebral vascular disease.

The third great category is comprised of sudden deaths due to meningococcic infections. A complete analysis of the extensive data in connection with this category probably does not fall within the province of this review. It is interesting, however, that in this very large group made up entirely of young adults, all of the symptomatology and physical signs included in the Waterhouse-Friderichsen syndrome, previously noted almost exclusively in children, were present in their fullest development. No effort was made to appraise the severity or functional significance of the myocardial involvement; the authors mention instances of focal, diffuse, and occasionally dense polymorphonuclear and monocyctic infiltration of the myocardium.

The fourth category is composed of 140 carefully investigated cases in which postmortem findings were negative. Very small or questionable coronary artery lesions were considered as negative findings. The majority of the soldiers showed only "agonal" changes, indicative of acute circulatory failure (acute systemic anoxia). It is entirely possible that unexplained poisoning may have been a factor in some cases, but circulatory death in most of them was apparently indisputable.

GOULEY.

Littman, D.: Electrocardiographic Phenomena Associated With Spontaneous Pneumothorax and Mediastinal Emphysema. Am. J. M. Sc. 212:682 (Dec.), 1946.

Two cases of mediastinal emphysema with spontaneous left-sided pneumothorax are described, and the electrocardiographic changes analyzed, together with those of similar cases reported in the literature. It is evident from these studies that gross electrocardiographic changes in the presence of mediastinal emphysema and left-sided pneumothorax are observed only in the CF leads, and can be obtained only when the patient is in the supine position. When the patient is in the prone, erect, or right lateral position the tracings are essentially normal. The CR leads are normal in any position, although the height of the T waves and size of the QRS excursions show variations. For these changes to occur it is necessary that the patient have both mediastinal emphysema and left-sided pneumothorax and the pneumothorax must be present in front of the heart. Thus the changes noted are not the result of interference with coronary filling as has been postulated by some, but rather, result from the presence of air between the heart and the exploring electrode, causing interference with electrical conduction. It is recommended that CF leads be made in various positions in the presence of spontaneous pneumothorax and mediastinal emphysema.

DURANT.

Stewart, H. J., Newman, A. A., and Evans, W. F.: Levels of Blood Pressure in Both Arms and Legs in Normal Subjects and Patients Suffering From Certain Disease. Am. J. Med. 1:451 (Nov.), 1946.

The authors confirm the observation made by other investigators; namely, that in normal subjects the systolic, diastolic, and pulse pressures are higher in the legs than in the arms. The pulse pressure in the legs is widened by a greater rise in systolic than in diastolic pressure.

In normal subjects the average systolic pressures in the legs exceeded that in the arms by 33.6 mm. Hg and the diastolic pressures in the legs exceeded the arm pressure by 25.1 millimeters. In thirteen patients with rheumatic mitral valve lesions, the average systolic and diastolic arm and leg pressures did not deviate significantly from those in normal subjects. In eleven patients with congenital heart disease the average systolic and diastolic arm pressures were not significantly different from those of normal subjects but the average systolic and diastolic leg pressures were only 11 to 13 mm. Hg higher than the pressures in the arms. Ten patients with Graves' disease averaged slightly higher systolic and diastolic pressures both in the arms and legs as compared with the normal subjects. Fifteen hypertensives had systolic leg pressures which averaged 43.5 mm. Hg higher than the pressure in the arms but the diastolic pressure averaged only 29 mm. Hg higher than the arm pressures. In eleven patients with rheumatic aortic insufficiency and mitral stenosis and insufficiency, the average systolic and diastolic pressures in the legs were higher than in the arms and the average pulse pressure differences in the legs were greater than in normal subjects and in patients with mitral valvular lesions alone.

The most significant differences were observed in patients with coarctation of the aorta. Of twenty-three patients, twenty-two exhibited systolic and diastolic pressures which were lower in the legs than in the arms. The authors emphasize the necessity for estimating the blood pressure in the legs of all patients with hypertension if patients with coarctation of the aorta are not to be overlooked.

FRIEDLAND.

Jervell, O.: Paroxysmal Tachycardia. Transitory Flutter and Fibrillation. Acta med. Scandinav. 125:295 (4), 1946.

Among 7,000 subjects studied electrocardiographically, from 1941 to 1944, there were 168 with paroxysmal arrhythmias. These included nine with "paroxysmal sinus tachycardia" (focus believed to be in the lower portion of the S.A. node), three with paroxysmal nodal rhythm, and one with paroxysmal ventricular tachycardia. The remainder had paroxysmal auricular flutter, fibrillation, or paroxysmal auricular tachycardia.

Seventy patients (thirty-three with fibrillation) had no evidence of organic heart disease or thyrotoxicosis. In many of these such possible predisposing factors as adiposity, infectious processes, recent exhausting exertion, chest deformity, pregnancy, and "digestive reflex neurosis"

were thought to be significant. Degenerative heart disease was diagnosed in sixty-seven, rheumatic heart disease in sixteen, and thyrotoxicosis in eleven of the patients with organically diseased hearts. The author believes that both a predisposing and a precipitating cause can be found in most instances of paroxysmal arrhythmia, the former being some organic or functional alteration of the auricular myocardium, and the latter a derangement of the autonomic nervous system, usually an increased sympathetic tone. SAYEN.

David, A. R., and Lipsitch, L. S.: Clinical Aspects of Calcification of the Mitral Annulus Fibrosus. Arch. Int. Med. 78:5 (Nov.), 1946.

The authors discuss the clinical aspects of calcification of the mitral annulus fibrosus and describe the physical signs and electrocardiographic changes that occurred during the life of ten such patients (ages 58 to 82 years). They point out that the lesion has been of incidental interest to the roentgenologist and pathologist. There was no evidence that the lesions in any of the cases presented were on a rheumatic basis; the etiologic factor seemed to be arteriosclerosis, which was invariably a marked finding.

The clinical findings revealed two cases of angina pectoris and five cases of congestive failure. Half of the patients reported showed complete heart block. It was interesting to note that seven of the ten patients had loud, rough systolic murmurs, and that four of the ten had blowing, apical diastolic murmurs (thought to be related to auricular activity). There was a definite correlation between the diastolic murmurs and the heart block. None of the murmurs were thought to be associated with either mitral stenosis or regurgitation.

It is believed that heart block may be expected when the calcification spreads into the septum, particularly when excrescences reach out from the ring to invade the conducting system more deeply.

The authors ventured to diagnose mitral annulus fibrosus on the basis of complete heart block, and apical diastolic murmur in elderly patients without a history of rheumatic fever. The diagnosis was confirmed by x-ray in three of the reported cases. HORWITZ.

Manlove, F. R.: Retinal and Choroidal Arterioles in Malignant Hypertension: A Clinical and Pathologic Study of Fifteen Cases. Arch. Int. Med. 78:4 (Oct.), 1946.

Manlove reviewed the literature on retinal and choroidal arteriolar changes in malignant hypertension, then discussed the clinical and pathologic changes found in fifteen patients between the age of 20 and 70 years (60 per cent of these patients were 50 years of age or over). In order of frequency, the symptoms were as follows: cardiac, central nervous system, general, visual, renal, and gastrointestinal. Of the fifteen patients, fourteen had albuminuria, four had casts in the urine, over half had a secondary anemia, and all had retention of urea and creatinine.

At autopsy, cardiac hypertrophy was an invariable finding, and in nearly every patient the kidneys were small and exhibited pitting and scarring of the surfaces. Sections of the eyes, cut to include the nerve head and macular area, were studied in the fifteen patients, as well as in seven controls. The vascular lesions included: 1. subendothelial proliferation of the arterioles of the choroid, but rarely of the retina; 2. medial thickening; 3. a perivascular fibrous tissue increase; 4. a varying degree of hyaline degeneration in the choroidal arterioles; and 5. occasional acute necrosis of the choroidal arterioles or infiltration of fat into the arteriolar wall.

There was also noted a marked reduction of the lumen-to-wall ratio in malignant hypertension, as compared to the controls. It is interesting to note that the percentage reduction from the normal mean was greater in the choroid and retina than in any other organ except the kidney. HORWITZ.

Rosenblueth, A., and Ramos, J. G.: The Various Components of the Monophasic Electrocardiogram of the Ventricle. Arch. Inst. cardiol. México 16:45 (Mar. 31), 1946.

The normal monophasic electrocardiograms of the ventricle of different animals (frog, turtle, cat, and dog) are similar and complex. They present several deviations or oscillations in the course of the main wave. These are modified independently by various experimental procedures. The assertion that the various oscillations are due to artefacts is refuted.

An evaluation of the factors which may produce the alternations of response leads to the conclusion that alternation of the electric phenomena may occur in a given group of active fibers and may even take place in a single fiber.

LUISADA.

Pallares, D. S., Paras, O., Cosio, E. C., and Mendoza, F.: The Intrinsic Deflection in Normal Cases and in Ventricular Hypertrophy. Arch. Inst. cardiol. México 16:397 (Oct. 31), 1946.

A study of the intrinsic deflection was made in 100 healthy persons. In every case the onset of the intrinsic deflection was earlier in leads taken from the right side than in leads from the left side of the precordium.

In only two normal cases, the intrinsic deflection was inscribed after 0.03 second in V_1 or V_2 ; in fourteen normal cases, the value of 0.045 second was exceeded in V_5 or V_6 .

The fact that in some normal persons the QRS complex is M-shaped in leads made with the chest electrode on the right side of the precordium and causes a delay in the onset of the intrinsic deflection shows the importance of caution in interpreting the value of the intrinsic deflection in V_1 or V_2 , where no other electrocardiographic abnormalities are noted.

One hundred tracings in which an onset of the intrinsic deflection in V_1 or V_2 occurred more than 0.03 sec. after the beginning of the ventricular complex were chosen at random. (Normal electrocardiograms and tracings showing right bundle branch block were excluded.) Rheumatic heart disease with mitral involvement was present in 91 per cent of the cases; chronic cor pulmonale was present in 5 per cent; tetralogy of Fallot in one per cent; congenital pulmonary stenosis in one per cent; luetic aortitis in one per cent; and arterial hypertension in one per cent. The patient with luetic aortitis showed pulmonary emphysema and dilatation of the right ventricle at autopsy. In every patient, except the patient with arterial hypertension, right ventricular hypertrophy was demonstrated by x-ray.

One hundred cases with an onset of the intrinsic deflection in V_5 or V_6 0.04 to 0.045 sec. after the beginning of the ventricular complex were studied. In 96 per cent of the cases some heart disease with hypertrophy of the left ventricle, shown by clinical or x-ray examination, was present. There were persons with normal hearts in this group.

One hundred cases with an onset of the intrinsic deflection in V_5 or V_6 0.045 to 0.05 sec. after the beginning of the QRS complex were studied. In 97 per cent, heart disease with left ventricular hypertrophy was present. Three persons with normal hearts were found in this group.

One hundred cases with the onset of the intrinsic deflection in V_5 or V_6 0.05 to 0.055 sec. after the beginning of the QRS complex were studied; 98 per cent showed evidence of heart disease and left ventricular hypertrophy. Fifty cases had rheumatic heart disease with aortic insufficiency. This finding is of help in proving or eliminating aortic insufficiency where there is a basal diastolic murmur without an accompanying high pulse pressure.

Twelve cases with a late intrinsic deflection in leads recorded from the right as well as the left side of the precordium were studied. All had advanced myocardial disease with diffuse ventricular enlargement.

Fifty cases with considerable left ventricular enlargement were studied. The intervals between the beginning of the QRS and the intrinsic deflection in V_5 or V_6 were as follows: 5 cases, 0.03 to 0.04 sec.; 18 cases, 0.04 to 0.05 sec.; 20 cases, 0.05 to 0.06 sec.; 5 cases, 0.06 to 0.07 sec.; one case above 0.07 sec., and one case in which the intrinsic deflection could not be determined. The comparison of these figures with the figures found in 100 normal cases strongly supports the view that the delay in the onset of the intrinsic deflection is produced by left ventricular hypertrophy.

In fifty cases with an x-ray showing right ventricular hypertrophy the interval between the beginning of the QRS complex and the onset of the intrinsic deflection in V_1 or V_2 was as follows: two cases, 0.01 to 1.02 sec.; 15 cases, 0.02 to 0.03 sec.; 14 cases, 0.03 to 0.4 sec.; 7 cases, 0.04 to 0.05 sec.; 3 cases, 0.07 to 0.08 sec.; and one case, 0.08 second. It is pointed out that in 60 per cent of these cases the onset of the intrinsic deflection occurs more than 0.03 sec. after the

beginning of the ventricular complex. These results are not so uniform as those that apply to the left ventricle, but they show deviations when compared with the results obtained in normal cases.

The study of the intrinsic deflection in the precordial leads has great value in the diagnosis of left ventricular hypertrophy. AUTHORS.

Klinefelter, E. W.: Significance of Calcification for Roentgen Diagnosis of Aneurysm of the Abdominal Aorta. Radiology 47:597 (Dec.), 1946.

The roentgen diagnosis of aneurysm of the abdominal aorta has been made in only 20 per cent of more than 1,000 cases recorded in the literature. The author presents three proven cases and discusses the diagnostic roentgen findings. The patients were all men, over 65 years of age, and suffered from chronic hypertension and far-advanced arteriosclerosis. The serology was negative in all three patients. One patient sustained a rupture of the aneurysm which, by the seepage of the blood retroperitoneally in the region of the rectum, produced filling defect of the rectum. This defect was demonstrated by barium enema. His chief complaint, over a period of six months, was pain in the right lower abdominal quadrant. The ruptured aneurysm was revealed when an operation was performed for suspected appendicitis. The other two patients presented no complaints directly referable to their aneurysms; one died of uremia secondary to prostatic carcinoma, the other died of coronary occlusion.

The diagnostic roentgen criteria, described in the literature, for aneurysm of the abdominal aorta are (1) vertebral erosion, (2) presence of a soft-tissue mass, (3) organ displacement, and (4) calcification. The author calls specific attention to the importance of differentiation between the calcification seen in the wall of the arteriosclerotic abdominal aorta and calcification in the wall of the aneurysm. In the former instance, the calcification tends to outline the length and width of the aorta through the major part of its course, while in the latter only a portion of the aneurysmal wall is outlined on the film by either a single, curved, continuous line or by a broken line of calcification; a considerable portion of the wall is ill-defined and requires careful study of the film to detect the indistinct calcification. MERANZE.

Leys, D.: Rheumatic Encephalopathy. Edinburgh M. J. 53:444 (August), 1946.

This author reports the presence in three girls, all at or past puberty, of acute rheumatic fever and chorea, associated with an unusual type of psychosis. Two of these patients were seen by a consulting psychiatrist, who diagnosed them as schizophrenic. All recovered sufficiently to resume active life and were in good health one year after the illness.

This author suggests that the three girls suffered from rheumatic encephalitis because puberty coincided with a period not only of prevalence of rheumatic fever but also with prevalence or enhancement of pathogenic neurotropic virus. Rheumatic psychosis of various types, including schizophrenia, has been described by neurologists or psychiatrists in studies of psychosis or encephalitis, but it does not seem to have been remarked by pediatricians. Chorea, or rheumatic encephalopathy, would appear to be very much modified by the age, sex, constitution, and experience of the victim, and very possibly by endocrine or biochemical factors. BELLET.

Govan, Clifton D., Jr.: The Effect of Salicylate Administration on the Prothrombin Time. J. Pediat. 29:629 (Nov.), 1946.

The author investigated the effect of varying doses of salicylates upon the prothrombin time in twenty-four children. Most of the patients were entirely well, three had acute rheumatic fever, and three suffered from acute hemorrhagic nephritis. Eighteen showed no significant change in prothrombin time, while six had abnormal prolongation. The most marked hypoprothrombinemia occurred between the second and the fifth day and in each of the six patients normal pretreatment levels were reached by the ninth day despite continuous salicylate administration. The prothrombin deficiency attending the therapeutic administration of salicylate is neither a constant nor a dangerous feature. The mechanism of hypoprothrombinemia production by salicylate is unknown; however it is most probably the result of changes in the liver effected by salicylate. HAUB.

Jackson, Robert L.: Heart Disease in Children in a Rural Town County; Particularly in Relation to Rheumatic Fever. J. Pediat. 29:647 (Nov.), 1946.

The calculated incidence of active rheumatic fever in the school population of Washington County, Iowa, was 0.61 per cent. The total incidence of organic heart disease was 0.47 per cent. The etiology of the organic disease was rheumatic in 58 per cent; the etiology in the remainder was congenital disease. These results were obtained as a by-product of a planned diagnostic survey conducted over the period of 1940 to 1945.

HAUB.

Faber, M.: The Cholesterol Content of the Human Aorta in Relation to the Serum Cholesterol Concentration. Acta med. Scandinav. 125:418, 1946.

The cholesterol content of a section of unit size, taken from the media and intima of the ascending aorta, was compared with the serum cholesterol content and correlated with age in normal persons (victims of death by accidental shooting), in hypertensive patients and, in patients with xanthomatosis. It was found that in normal persons the aortic cholesterol content rose slowly with advancing age but showed no parallel with the serum content. In essential hypertension the aortic cholesterol increased at a more rapid rate than in normal individuals but the serum content did not; whereas the xanthomatosis cases studied showed a rise in both aortic and serum cholesterol.

SAYEN.

Kjergaard, H.: Patent Ductus Botalli in Three Sisters. Acta Med. Scandinav. 125:339, 1946.

The author reports three cases of patent ductus arteriosus in a family that included five children. He suggests that the rarity of reports of similar occurrences in the literature may be due to failure to examine thoroughly all members of families in which a case of congenital heart disease has been discovered.

SAYEN.

van Buchem, F. S. P.: Extensive Calcification in the Heart at an Early Age. Acta med. Scandinav. 125:182, (d) 1946.

A girl, 18 years of age, with a three-year history of many painless collapses after overexertion, excitement, or passage from a cold to a warm environment, developed exertional interscapular pain with bilateral arm radiation to the arms and, finally, congestive heart failure, from which she died. Her blood pressure was 135-90. Cyanosis of hands and feet was present. The Electrocardiogram showed right axis deviation and RS-T segment depression in Leads II, III, and IVF. Serum calcium was 13.2 mg. per 100 ml. and serum cholesterol, 223.

Necropsy showed marked right ventricular hypertrophy and extensive calcification in the endocardial and subendocardial musculature of the left ventricle. The coronary arteries were normal. No conclusive explanation for the calcification could be found but it was proposed that the left ventricular endocardium had been injured by previous exertion and that calcium had been deposited at the sites.

SAYEN.

Frost, J.: A Comparison Between the Leads from the Extremities, the Precordial Leads CF₂ and IVF, and Nehb's Leads, With Special Regard to the Diagnosis of Infarction. Acta med. Scandinav. 125:15, 1946.

In a study of 221 persons, 110 with heart disease, including 25 with myocardial infarction (eight autopsies), comparisons were made of the relative value of limb leads, chest leads (CF₂ and IVF) and Nehb leads. The latter were taken from the angles of a triangle formed by points in the second left intercostal space anteriorly near the sternum, the cardiac apex, and the projection of the apex in the posterior axillary line. It was found in rare cases that Nehb's "D" Lead (exploring electrode posteriorly, indifferent electrode in the second left intercostal space) showed an abnormal pattern when Leads II and III did not, and might, therefore, be used as a

supplement to the standard leads in the diagnosis of posterior infarction. Usually Nehb's leads revealed no abnormalities that were not revealed also in the limb leads, CF₂ and IVF. The importance of serial tracings and the value of taking Leads CF₃ and CF₅ in addition to the Nehb and other leads are stressed.

SAYEN.

Gilbert, R. A., and Goldzieher, J. W.: The Mechanism and Prevention of Cardiovascular Changes Due to Insulin. *Ann. Int. Med.* 25:928 (Dec.), 1946.

Following the administration on different days of insulin alone, of insulin with prostigmin, and of adrenalin alone, the authors studied the effects on the cardiovascular systems of three healthy young adults and of five patients over 50 years of age with diminished cardiac reserve. They employed insulin with adequate amounts of glucose to prevent any lowering of the blood sugar in 10 other subjects used as controls. Their results indicated that either insulin (only when hypoglycemia is allowed to develop) or adrenalin will augment the heart rate and blood pressure in all subjects and, in those with an already lowered cardiac reserve, will also elevate the venous pressure and reduce blood velocity. They also observed that these effects induced by insulin hypoglycemia are prevented by the supplemental administration of prostigmin. Finally, it was observed that analagous changes in the ST segment and T waves of the electrocardiogram occurred in those with diminished cardiac reserve following the administration of either insulin or adrenalin alone. This latter phenomenon is interpreted by the authors to signify that electrocardiographic changes evoked by insulin are to be related to heightened sympathetic activity reflexly induced by the hypoglycemia.

WENDKOS.

de la Barrera, P., and de Molina, A. F.: Conclusions Based Upon Experiments With Hypertension in a Dog, Hypertension in a Cow, and Pepsin. *Rev. clin. españ.* 23:114 (Oct. 31), 1946.

Renin, obtained from the plasma of a dog free from hypertensinase, does not raise the blood pressure in a normal anesthetized dog, when injected with hypertensinogen of a cow. Inconclusive results are obtained when the plasma is incubated with dog's hypertensinogen.

Renin extracts obtained from calf kidney cortex and incubated with dog's hypertensinogen did not produce hypertension. The same calf's renin when incubated with cow's hypertensinogen always produced a hypertensive effect.

Dog's renin incubated with dog's hypertensinogen produced hypertension.

The extracts obtained by incubation of pepsin with cow's hypertensinogen produced variable effects. The same extracts incubated with dog's hypertensinogen were ineffective.

It was concluded, therefore, that a specificity of the renin-hypertensinogen reaction does exist. In studying the comparative changes of the plasma hypertensinogen, the need to use renin obtained from kidneys of the same animal species is pointed out.

AUTHORS.

Salazar Mallén, M., and Madel Refugio Balcàzar, Q. B. P.: Influence of Sodium Salicylate on the Antigen-Antibody Reaction. *Arch. Inst. cardiol. México* 16:432 (Oct. 31), 1946.

The author studied the action of sodium salicylate, both in an albumin-antialbumin and in a streptolysin-antistreptolysin system. The specific precipitates are inhibited in vitro by sodium salicylate. This action is specific because a similar effect is not obtained with antipyrine.

Sodium salicylate seems to combine with the antistreptolysin, thereby interfering with the possible neutralization of streptolysin.

LUISADA.

American Heart Association, Inc.

1790 BROADWAY, NEW YORK 19, N. Y.

Telephone Circle 5-8000

OFFICERS

<i>Vice-President</i>	<i>President</i>	<i>Secretary</i>
DR. ARLIE R. BARNES	DR. HOWARD F. WEST	DR. HOWARD B. SPRAGUE
<i>Treasurer</i>	<i>Acting Executive Secretary</i>	<i>Acting Medical Director</i>
DR. GEORGE R. HERRMANN	DR. H. M. MARVIN	DR. DAVID D. RUTSTEIN

DIRECTORS

DR. EDGAR V. ALLEN.....	Rochester, Minn.	DR. HAROLD E. B. PARDEE.....	New York City
DR. GRAHAM ASHER.....	Kansas City, Mo.	DR. WILLIAM B. PORTER.....	Richmond, Va.
*DR. ARLIE R. BARNES.....	Rochester, Minn.	*DR. DAVID D. RUTSTEIN.....	New York City
DR. ALFRED BLALOCK.....	Baltimore	*DR. JOHN J. SAMPSON.....	San Francisco
*DR. WILLIAM H. BUNN.....	Youngstown, Ohio	DR. ROY W. SCOTT.....	Cleveland
DR. CLARENCE DE LA CHAPELLE.....	New York City	*DR. HOWARD B. SPRAGUE.....	Boston
*DR. TINSLEY R. HARRISON.....	Dallas	DR. GEORGE F. STRONG.....	Vancouver, B. C., Can.
DR. GEORGE R. HERRMANN.....	Galveston	DR. WILLIAM D. STROUD.....	Philadelphia
DR. T. DUCKETT JONES.....	Boston	DR. HOMER F. SWIFT.....	New York City
DR. LOUIS N. KATZ.....	Chicago	DR. WILLIAM P. THOMPSON.....	Los Angeles
DR. SAMUEL A. LEVINE.....	Boston	DR. HARRY E. UNGERLEIDER.....	New York City
DR. GILBERT MARQUARDT.....	Chicago	*DR. HOWARD F. WEST.....	Los Angeles
*DR. H. M. MARVIN.....	New Haven	DR. PAUL D. WHITE.....	Boston
*DR. EDWIN P. MAYNARD, JR.....	Brooklyn	DR. FRANK N. WILSON.....	Ann Arbor
*DR. THOMAS M. McMILLAN.....	Philadelphia	*DR. IRVING S. WRIGHT.....	New York City
DR. JONATHAN MEAKINS.....	Montreal, Can.	DR. WALLACE M. YATER.....	Washington, D. C.
DR. E. STERLING NICHOL.....	Miami		

*Executive Committee.

THE American Heart Association was founded in 1924 "for the study of and the dissemination and application of knowledge concerning the causes, treatment and prevention of heart disease; the gathering of information on heart disease; the development and application of measures that would prevent heart disease; seeking and provision of occupations suitable for heart disease patients; the promotion of the establishment of special dispensary classes for heart disease patients; the extension of opportunities for adequate care of cardiac convalescents; the promotion of permanent institutional care for such cardiac patients as are hopelessly incapacitated from self-support; and the encouragement and establishment of local associations with similar objects throughout the United States."

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The American Council on Rheumatic Fever, organized in 1944, consists of a group of representatives of all national medical organizations concerned with rheumatic fever. It operates administratively through the American Heart Association and carries out the program of the American Heart Association insofar as that relates to rheumatic fever.

Annual membership in the American Heart Association is \$2.50 and includes twelve issues of *Modern Concepts of Cardiovascular Disease*; Journal membership is \$10.00 and includes a year's subscription to the AMERICAN HEART JOURNAL (January-December), twelve issues of *Modern Concepts of Cardiovascular Disease*, and annual membership in the Association. Contributing membership starts at \$25.00 per year; patron membership is \$50.00 and over per year. Membership blanks will be sent upon request.

The Association earnestly solicits your support and suggestions for its work. Donations will be gratefully received and promptly acknowledged.

AMERICAN HEART JOURNAL

For the Study of the
CIRCULATION



©Am. Ht. Assn.

PUBLISHED MONTHLY

Under the Editorial Direction of
THE AMERICAN HEART ASSOCIATION

THOMAS M. McMILLAN

Editor-in-Chief

ASSOCIATE EDITORS

WALLACE M. YATER

SAMUEL BELLET

LOUIS B. LAPLACE

EDITORIAL BOARD

EDGAR V. ALLEN

ALFRED BLALOCK

CLARENCE E. DE LA CHAPELLE

HARRY GOLDBLATT

TINSLEY R. HARRISON

T. DUCKETT JONES

LOUIS N. KATZ

EUGENE M. LANDIS

JOHN K. LEWIS

H. M. MARVIN

JONATHAN C. MEAKINS

ROY W. SCOTT

ISAAC STARR

PAUL D. WHITE

FRANK N. WILSON

CHARLES C. WOLFERTH

IRVING S. WRIGHT

VOLUME 33

JANUARY-JUNE, 1947

St. Louis

THE C. V. MOSBY COMPANY

1947

COPYRIGHT 1947, BY THE C. V. MOSBY COMPANY

(All rights reserved)

Printed in the
United States of America

*Press of
The C. V. Mosby Company
St. Louis*

INDEX TO VOLUME 33

AUTHORS INDEX

A

- ABRAMSON, DAVID I., AND SHUMACKER, HARRIS B. Raynaud's disease in men, 500
- ADAMSON, W. B. Is the orthodox therapy of rheumatic fever conducive to psychosomatic disability? 715
- ADOLPH, WILLIAM. (See Winsor, Adolph, Ralston, and Leiby), 704
- AIXALA, RAMON. The apex cardiogram and its utility in phonocardiography, 703
- ALBERTI, V. J. (See Vaccarezza, Croxatto, and Alberti), 728
- ALTSCHULE, M. D., AND SULZBACH, W. M. Tolerance of the human heart to acidosis; reversible changes in RS-T interval during severe acidosis caused by administration of carbon dioxide, 458
- ANDERSON, HAROLD C. (See Geiger and Anderson), 240
- ARAYA, EMILIO. (See Battro and Araya), 723
- ASHMAN, RICHARD. (See Byer, Ashman, and Toth), 796

B

- BAER, L. S. (See McGinty and Baer), 102
- BARROSO-MOGUEL, ROSARIO. (See Costero and Barroso-Moguel), 701
- BATTO, ANTONIO, AND ARAYA, EMILIO. Importance of precordial leads in electrocardiograms after exertion in angina pectoris; action of certain drugs (trinitrin, aminophylline, and papaverine), 723
- , AND BIDOGGIA, HECTOR. Endocardiac electrocardiogram obtained by heart catheterization in the man, 604
- BAYLEY, ROBERT H. (See First, Stickle, and Bayley), 1
- BEAN, WILLIAM B. (See Eichna, Horvath, and Bean), 254
- BEN-ASHER, SOLOMON. Further observations on the treatment of the anginal syndrome with thiouracil, 490
- BERBER, SAMUEL. Report of a case of tricuspid insufficiency of the Ebstein type with probable fetal endocarditis and exceptional electrocardiographic characteristics, 726
- BERCONSKY, ISAAC. (See Cossio and Berconsky), 720
- , AND NEUMAN, J. Cardiac asthma and acute edema of the lungs in mitral stenosis with auricular fibrillation, 738

- BERGMAN, H. C. (See Prinzmetal, Simkin, Bergman, and Kruger), 420
- BIDOGGIA, HECTOR. (See Battro and Bidoggia), 604
- BLALOCK, ALFRED. (See Taussig and Blalock), 413
- BORGES, S. (See Ramos, de Melo, and Borges), 699
- BOSCO, GUILLERMO. Critical examination of the current classification of the localization of myocardial infarcts (the author's terminology), 722
- BREIDENBACH, WARREN C., JR., AND PALMER, DWIGHT M. Thromboangiitis obliterans in the Negro: report of a case and review of the literature, 849
- BRENES, MARIO. (See Salazar Mallen, Lozano, and Brenes), 692
- BROWN, ELLEN. (See Sampson, Brown, and Hopper), 703
- BURCH, G. E. A new sensitive portable plethysmograph, 48
- BYER, EDWIN, ASHMAN, RICHARD, AND TOTH, LOUIS A. Electrocardiograms with large, upright T waves and long Q-T intervals, 796

C

- CABRERA, ENRIQUE. (See Sodi Pallares, Vizcaino, Soberon, and Cabrera), 819
- CAIN, EDMUND F. Wolff-Parkinson-White syndrome presenting certain unusual features, 523
- CARLOTTI, JACQUES, HARDY, IRAD B., JR.; LINTON, ROBERT R., AND WHITE, PAUL D. Pulmonary embolism in medical patients: a comparison of incidence, diagnosis, and the effects of treatment of 273 cases at the Massachusetts General Hospital in two five-year periods (1936 to 1940 and 1941 to 1945 inclusive), 737
- CASTANEDA, R. (See Meneses Hoyos, Castaneda, and Mingram), 706
- CASTELLANOS, AUGUSTIN. (See de los Reyes and Castellanos), 727
- CAVALHEIRO DIAS, J. (See Decourt, Ramos, Jr., Tranchesi, Corea, Cavaleiro Dias, and Tisi), 697
- CELIS, ALEJANDRO. (See Chavez, Dorbecker, and Celis), 560
- CHAPMAN, BERNARD M. (See Ware and Chapman), 530

- CHAVEZ, IGNACIO, DORBECKER, NARNO, AND CELIS, ALEJANDRO. Direct intracardiac angiocardiology—its diagnostic value, 560
- CHESNUT, JOHN L. (See Meneely and Chesnut), 175
- COHN, ROY. An experimental method for the closure of interauricular septal defects in dogs, 453
- COOLEY, MAHLON C. The treatment of congestive heart failure, 740
- COREA, IGNACIO A. (See Decourt, Ramos, Jr., Tranchesi, Corea, Cavalheiro Dias, and Tisi), 697
- CORTES, C., AND VILLARREAL, HERNAN. Clinical features of 1,160 cases of rheumatic valvular endocarditis, 715
- COSSIO, PEDRO. The first cardiac sound in premature contractions, 707
- , AND BERCONSKY, ISAAC. Post-tachycardia syndrome, 720
- COSTERO, ISAAC. (See de Gortari, Pellon, and Costero), 716
- , The significance of interstitial lymphocytosis in rheumatic disease and in other inflammatory processes, 717
- , AND BARROSO-MOGUEL, ROSARIO. Alterations in the structure of the liver cell in congestive heart failure, 701
- CROXATTO, LANARI. (See Vaccarezza, Croxatto, and Alberti), 728

D

- DECOURT, LUIS V., RAMOS, JOSE, JR., TRANCHESI, BERNARDINO, COREA, IGNACIO A., CAVALHEIRO DIAS, J., AND TISI, GASPARE. Chronic heart involvement in Chagas' disease, 697
- DE GORTARI, ALFONSO, PELLON, RUBEN, AND COSTERO, ISAAC. Encephalopathy of the rheumatic patient, 716
- DE LA CHAPPELLA, CLARENCE E. (See Kossmann, Goldwater, and de la Chapella), 700
- DE LOS REYES, PEREZ, AND CASTELLANOS, AUGUSTIN. Classification of congenital heart diseases, 727
- DE MELO, H. K. (See Ramos, de Melo, and Borges), 699
- DENOLIN, H. (See Segers, Lequime, and Denolin), 685
- DEZA, D. (See Rojas and Deza), 702
- DORBECKER, NARNO. (See Chavez, Dorbecker, and Celis), 560
- DURANT, THOMAS M., LONG, JOAN, AND OPPENHEIMER, MORTON J. Pulmonary (venous) air embolism, 269
- DWORIN, MILTON. (See Geffer, Leaman, Lucchesi, Maher, and Dworin), 228

E

- EICHNA, LUDWIG W., HORVATH, STEVEN M., AND BEAN, WILLIAM B. Cardiac asystole in a normal young man following physical effort, 254

- ELEK, STEPHEN R. (See Nathanson and Elek), 464
- ELLIS, GEORGE M. Dissecting aneurysm with hemopericardium, 860

F

- FEIGIN, IRWIN. (See Rosenthal and Feigin), 346
- FELDMAN, D. (See Katz, Feldman, and Langendorf), 696
- , (See Katz, Malinow, Kondo, Feldman, and Grossman), 319
- FIRST, SAFETY R., STICKLE, ARTHUR W., AND BAYLEY, ROBERT H. Electrocardiographic studies in rheumatic heart disease with reference to interpretation of multiple unipolar precordial leads, 1
- FREEMAN, NORMAN E. The diagnosis and treatment of thromboangiitis obliterans in the vascular centers of Army General Hospitals, 332

G

- GARCIA CARRILLO, E. The cardiac action of Central American snake venom, 709
- GARCIA RAMOS, J. (See Rosenblueth and Garcia Ramos), 677
- GARVIN, JUSTIN A., AND KLINE, EDWARD M. Congenital paroxysmal tachycardia, 362
- GASPARY, FERNANDO. (See Gonzalez Sabathie and Gaspary), 720, 729, 732
- GEEVER, E. F., AND RAVIN, A. Single coronary artery, 538
- GEFFER, WILLIAM I., LEAMAN, WILLIAM G., JR., LUCCHESI, PASCAL F., MAHER, IRENE E., AND DWORIN, MILTON. The heart in acute anterior poliomyelitis, 228
- GEIGER, ARTHUR J. Experiences in the treatment of subacute bacterial endocarditis with penicillin, 736
- , AND ANDERSON, HAROLD C. Lutembacher's syndrome complicated by acute bacterial endocarditis, 240
- GOLDBERG, HAROLD H. (See Kossmann and Goldberg), 308
- GOLDWATER, LEONARD J. (See Kossmann, Goldwater, and de la Chapella), 700
- GOMEZ DEL CAMPO, C., AND MENESES HOYOS, J. Angiography of the aorta, 729
- GONZALEZ SABATHIE, L. Morphine treatment of acute pulmonary edema, 738
- , On the intravenous use of morphine in the treatment of paroxysmal ventricular tachycardia, 719
- , AND GASPARY, FERNANDO. Auricular prefibrillation, 720
- , AND —, Sinoauricular block, 732
- GONZALEZ SABATHIE, LUIS, AND GASPARY, FERNANDO. Benign residual arrhythmias, 729
- GONZALEZ TOMAYO, A. (See Meneses Hoyos and Gonzalez Tomayo), 698

- GRANT, ROBERT P. Congestive heart failure and death in a case of paroxysmal auricular tachycardia, 121
- GROLLMAN, ARTHUR. The pathogenesis and treatment of hypertension, 721
- GROSS, ROBERT E. (See Reifenstein, Levine, and Gross), 146
- GROSSMAN, N. (See Katz, Malinow, Kondo, Feldman, and Grossman), 319
- GUBNER, RICHARD. (See Ungerleider and Gubner), 807
- GUERRA, F. Significance of ventricular oxygen consumption and of the enzymatic liberation of phosphorus in the mechanism of digitalis effect, 705

H

- HAFKESBRING, ROBERTA, AND WERTENBERGER, GRACE E. The effect of sulfonamide administration on cardiac function in the dog, 84
- HAMILTON, BURTON E. Report from the cardiac clinic of the Boston Lying-in Hospital for the first twenty-five years, 663
- HANSEN, ANDERS TYBJAERG, AND WARBURG, ERIK. An improved electric manometer for measuring the intra-arterial, intravenous, and intracardial pressure, with a general theory of manometers, 709
- HARDY, IRAD B., JR. (See Carlotti, Hardy, Jr., Linton, and White), 737
- HEDLUND, S. (See Nylin and Hedlund), 770
- HELLERSTEIN, H. K., AND MARTIN, JOHN W. Incidence of thromboembolic lesions accompanying myocardial infarction, 443
- HERRMANN, GEORGE R. Experimental and clinical studies in hypercholesterolemia and atherosclerosis and the effect of decholesterolizing agents, 711
- HERVE, LUIS. Medical-social features of heart disease in Chile, 710
- HIMWICH, H. E. (See Randles, Himwich, Homburger, and Himwich), 341
- HIMWICH, W. A. (See Randles, Himwich, Homburger, and Himwich), 341
- HOMBURGER, E. (See Randles, Himwich, Homburger, and Himwich), 341
- HOPPER, J. J. (See Sampson, Brown, and Hopper), 703
- HORVATH, STEVEN M. (See Eichna, Horvath, and Bean), 254
- HORWITZ, ORVILLE. A case of large overdose of epinephrine, 107
- HULL, EDGAR. (See Levy, II, and Hull), 856

I

- ISBERG, EMIL M. (See Peet and Isberg), 735

J

- JIMENES ROMO, FLAVIO. Penicillin in the treatment of subacute bacterial endocarditis: further studies in twenty-one patients, 736

- JOHNSON, EVELYN. (See Shapiro and Johnson), 725

- JOHNSTON, FRANKLIN D. (See Wilson, Johnston, Kossmann), 594

- JORDAN, FRED C., AND RANDOLPH, HOWELL. Congenital complete heart block diagnosed in utero with sound tracings and simultaneous electrocardiograph of the mother, 109

K

- KATZ, L. N. (See Kondo, Katz, Meyer, and Malinow), 207

- , FELDMAN, D., AND LANGENDORF, R. The diagnostic value of electrocardiographic patterns based on an assay of 261 additional autopsied cases, 696

- , MALINOW, M. R., KONDO, B., FELDMAN, D., AND GROSSMAN, N. The volume elasticity of the aorta in the intact dog, 319

- KAUNITZ, PAUL E. Origin of left coronary artery from pulmonary artery, 182

- KERR, W. J. The differential diagnosis of aortic stenosis, pulmonary stenosis, patent ductus arteriosus, and coarctation of the aorta, 725

- KLEIN, ARTHUR. Spontaneous mediastinal emphysema with acute right ventricular strain, 867

- KLINE, EDWARD M. (See Garvin and Kline), 362

- KONDO, B. (See Katz, Malinow, Kondo, Feldman, and Grossman), 319

- , KATZ, L. N., MEYER, J., AND MALINOW, M. R. The plethysmographic measurement of blood flow through the forepaw during experimental shock, 207

- KOSSMANN, CHARLES E. (See Wilson, Johnston, and Kossmann), 594

- , AND GOLDBERG, HAROLD H. Sequence of ventricular stimulation and contraction in a case of anomalous atrioventricular excitation, 308

- , GOLDWATER, LEONARD J., AND DE LA CHAPPELLA, CLARENCE E. Selective placement of patients with heart disease in competitive employment, 700

- KRAMER, LOUIS I. (See Zimdahl and Kramer), 218

- KRUGER, H. E. (See Prinzmetal, Simkin, Bergman, and Kruger), 420

L

- LANGENDORF, R. (See Katz, Feldman, and Langendorf), 696

- , (See Malinow and Langendorf), 705

- , Concealed A-V conduction: the effect of blocked impulses on the formation and conduction of subsequent impulses, 731

- , AND PIRANI, C. L. The heart in uremia, 282

- LANGLEY, ROBERT W. (See Reed, Langley, and Utz), 701
 —, REED, JOSEPH C., AND UTZ, DAVID C. Bundle branch block: a review of 100 cases, 730
 LAPIN, ALBERT W. Significance of abnormally small QRS deflections in one or more precordial leads, 747
 LASKY, I. I. (See Yettra and Lasky), 516
 LAUBRY, CH., AND ROUTIER, D. Heart disease and pregnancy, 739
 LEAMAN, WILLIAM G. (See Geffer, Leaman, Lucchesi, Maher, and Dworin), 228
 LEIBY, GEORGE M. (See Winsor, Adolph, Ralston, and Leiby), 704
 LEQUIME, J. (See Segers, Lequime, and Denolin), 685
 LEVINE, SAMUEL A. (See Reifstein, Levine, and Gross), 146
 LEVY BOLADERES, J. (See Martinez de la Cruz and Levy Boladeres), 733
 LEVY, LOUIS, II, AND HULL, EDGAR. Perforation of the interventricular septum in a case of subacute bacterial endocarditis, 856
 LINTON, ROBERT R. (See Carlotti, Hardy, Jr., Linton, and White), 737
 LONG, JOAN. (See Durant, Long, and Oppenheimer), 269
 LOZANO, HUBE E. (See Salazar Mallen, Lozano, and Brenes), 692
 LUCCHESI, PASCAL F. (See Geffer, Leaman, Lucchesi, Maher, and Dworin), 228

M

- McGINTY, A. P., AND BAER, L. S. Effect on the heart of an overdose of epinephrine, 102
 MCGOVERN, TERESA. Clinical impression of the therapy in thromboangitis obliterans, 712
 MACLAUGHLIN, JAMES A. (See Weisberger and MacLaughlin), 27
 MADDUX, KEMPSON. Intermittent ventricular tachycardia in youth. Report of case with fatal termination, 739
 MAHAIM, IVAN. Kent's fibers and the A-V paraspecific conduction through the upper connections of the bundle of His-Tawara, 651
 MAHER, IRENE E. (See Geffer, Leaman, Lucchesi, Maher, and Dworin), 228
 MALINOW, M. R. (See Katz, Malinow, Kondo, Feldman, and Grossman), 319
 —. (See Kondo, Katz, Meyer, and Malinow), 207
 —, AND LANGENDORF, R. Different mechanisms of fusion beats, 705
 MARTIN, JOHN W. (See Hellerstein and Martin), 443
 MARTINEZ DE LA CRUZ, F., AND LEVY BOLADERES, J. Arterial hypertension—its medical and surgical aspects, 733
 MASTER, ARTHUR M. Incidence of acute coronary artery occlusion, 135
 MATHISEN, A. K., AND PALMER, J. D. Diffuse scleroderma with involvement of the heart, 366
 MENDEZ HERNANDEZ, LUIS. Study of cerebral and peripheral emboli registered in the National Institute of Cardiology of Mexico, from September, 1944, to May, 1946, 712
 MENEELY, GEORGE R., AND CHESNUT, JOHN L. A relation between the size of the heart and the velocity of the blood, 175
 MENESES HOYOS, J. (See Gomez del Campo and Meneses Hoyos), 729
 —. An easy method for calculating the value of the medium axis and the ventricular gradient, 699
 —, CASTANEDA, R., AND MINGRAM, R. Studies on the heart sound in mitral stenosis, 706
 MENESES HOYOS, JORGE, AND GONZALEZ TOMAYO, A. Comparative study of different precordial leads, 698
 MEYER, J. (See Kondo, Katz, Meyer, and Malinow), 207
 MIDDLETON, WILLIAM S., AND RITCHIE, GORTON. The tetralogy of Fallot, 250
 MILLER, RALPH. (See Perelman and Miller), 34
 MINGRAM, R. (See Meneses Hoyos, Castaneda, and Mingram), 706
 MITCHELL, NATHAN. Arteriosclerotic aneurysm of the cardiac coronary arteries, 112

N

- NATHANSON, MORRIS H., AND ELEK, STEPHEN R. The influence of heart size on the circulation time, 464
 NEUMAN, J. (See Berconsky and Neuman), 738
 NICHOL, E. STERLING. Treatment of acute coronary thrombosis with dicumarol: further observations, 722
 NUZUM, FRANKLIN R. Hernia of esophageal hiatus: its relationship to angina pectoris, 724
 NYLIN, G., AND HEDLUND, S. Weight of the red blood corpuscles in heart failure determined with labelled erythrocytes during and after decompensation, 770

O

- OPPENHEIMER, MORTON J. (See Durant, Long, and Oppenheimer), 269

P

- PALMER, DWIGHT M. (See Breidenbach, Jr., and Palmer), 849
 PALMER, J. D. (See Mathisen and Palmer), 366
 PEET, MAX M., AND ISBERG, EMIL M. The role of surgical treatment in the management of hypertension, 735

- PELLON, RUBEN. (*See de Gortari, Pellon, and Costero*), 716
- PENNER, SIDNEY L. (*See Peters and Penner*), 528
- PERELMAN, JULIUS S., AND MILLER, RALPH. Atrionodal rhythm with ventricular bigeminy, 34
- PETERS, MICHAEL, AND PENNER, SIDNEY L. Pulmonary edema in the pregnant patient with mitral stenosis, 528
- PIRANI, C. L. (*See Langendorf and Pirani*), 282
- POE, WILLIAM D. Fatal coronary artery disease in young men, 76
- PRINZMETAL, MYRON, SIMKIN, BENJAMIN, BERGMAN, H. C., AND KRUGER, H. E. Studies on the coronary circulation. II. The collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres, 420
- PUIG SOLANES, M. Retinal angioscopy in essential arterial hypertension (a study of 300 clinical cases), 733

R

- RAAB, W. Sympathomimetic amines in the heart muscle: their pathogenic and therapeutic significance, 707
- RALSTON, WALTER C. (*See Winsor, Adolph, Ralston, and Leiby*), 704
- RAMOS, J., DE MELO, H. K., AND BORGES, S. Comparative studies with the three types of electrocardiographic leads (classic, unipolar extremity leads, and multiple precordial leads) in relation to clinical and radiologic examinations, 699
- RAMOS, JOSE, JR. (*See Decourt, Ramos, Jr., Tranchesi, Corea, Cavalheiro Dias, and Tisi*), 697
- RANDLES, F. S., HIMWICH, W. A., HOMBURGER, E., AND HIMWICH, H. E. The influence of vitamin B₁ deficiency on the pyruvate exchange of the heart, 341
- RANDOLPH, HOWELL. (*See Jordan and Randolph*), 109
- RAVIN, A. (*See Geever and Ravin*), 538
- REED, JOSEPH C. (*See Langley, Reed, and Utz*), 730
- , LANGLEY, ROBERT W., AND UTZ, DAVID C. A review of eight cases of Wolff-Parkinson-White syndrome including four cases with initial left ventricular activation as demonstrated by the multiple precordial leads, 701
- REIFENSTEIN, GEORGE H., LEVINE, SAMUEL A., AND GROSS, ROBERT E. Coarctation of the aorta, 146
- RITCHIE, GORTON. (*See Middleton and Ritchie*), 250
- RIVERO CARBALLO, J. M. (*See Sodi Pallares, Velez Orozco, and Rivero Carballo*), 705

- RIVERO CARVALLO, J. M. A new diagnostic sign of tricuspid insufficiency, 728
- ROBLES GIL, J. Incidence and clinical features of rheumatic fever in Mexico City, 713
- ROJAS, R. A., AND DEZA, D. Cardiac changes in malarial patients, 702
- ROSENBLUETH, A., AND GARCIA RAMOS, J. Studies on flutter and fibrillation. II. The influence of artificial obstacles on experimental auricular flutter, 677
- ROSENTHAL, JULIUS, AND FEIGIN, IRWIN. Pathology of the mitral valve in the older age groups, 346
- ROTH, GRACE M., AND SHEARD, CHARLES. The effect of smoking on the vasodilatation produced by the oral administration of 95 per cent ethyl alcohol or a substantial meal, 654
- ROTTA, ANDRES. Physiologic condition of the heart in the natives of high altitudes, 669
- ROUTIER, D. (*See Laubry and Routier*), 739

S

- SALANS, A. HARVEY, AND TWEED, PHYLLIS. A preliminary study of the coronary circulation post mortem, 477
- SALAZAR MALLÉN, M., LOZANO, HUBE E., AND BRENES, MARIO. Comparative study of blood cultures made from artery, vein, and bone marrow in patients with subacute bacterial endocarditis, 692
- SAMPSON, J. J., BROWN, ELLEN, AND HOPPER, J. J. Circulatory changes resulting from obstetric labor, 703
- SCHWARTZ, WILLIAM B. The treatment of shock accompanying myocardial infarction, 169
- SEGALL, HAROLD N. On writing symbols to describe cardiovascular sounds and murmurs while listening, 705
- SEGBERS, M., LEQUIME, J., AND DENOLIN, H. Synchronization of auricular and ventricular beats during complete heart block, 685
- SHAPIRO, M. J., AND JOHNSON, EVELYN. Results of surgery in patent ductus arteriosus, 725
- SHEARD, CHARLES. (*See Roth and Sheard*), 654
- SHUMACKER, HARRIS B. (*See Abramson and Shumacker*), 500
- SIMKIN, BENJAMIN. (*See Prinzmetal, Simkin, Bergman, and Kruger*), 420
- SMITH, HARRY L. Attacks of unconsciousness resulting from hyperactive carotid sinus reflex, 711
- SOBERON, JORGE. (*See Sodi Pallares, Vizcaino, Soberon, and Cabrera*), 819
- SODI PALLARES, DEMETRIO, VIZCAINO, MARIO, SOBERON, JORGE, AND CABRERA, ENRIQUE. Comparative study of the intracavity potential in man and in dog, 819

- SODI PALLARES, E., VELEZ OROZCO, F., AND RIVERO CARBALLO, J. M. Note on a pentose isolated from heart muscle, 705
- STICKLE, ARTHUR W. (*See* First, Stickle, and Bayley), 1
- STRASSMANN, GEORGE. Traumatic rupture of the aorta, 508
- SUAREZ, RAMON M. Electrocardiographic studies in Puerto Rico with unipolar precordial leads in normal individuals of both sexes and at different ages, 731
- SULZBACH, W. M. (*See* Altschule and Sulzbach), 458
- SUTTON, DON C. Cardiac pain, 724
- SZILAGYI, NELLY. (*See* Taran and Szilagyi), 14

T

- TAQUINI, ALBERTO C. Cardiac failure in tricuspid disease, 727
- . Fagarine—a new drug for the treatment of auricular fibrillation and flutter, 719
- . Value of the pressor test in high blood pressure, 735
- TARAN, LEO M., AND SZILAGYI, NELLY. The duration of the electrical systole (Q-T) in acute rheumatic carditis in children, 14
- TAUSSIG, HELEN B., AND BLALOCK, ALFRED. Observations on the volume of the pulmonary circulation and its importance in the production of cyanosis and polycythemia, 413
- TISI, GASPAR. (*See* Decourt, Ramos, Jr., Tranchesi, Corea, Cavaleiro Dias, and Tisi), 697
- TORO VILLA, GABRIEL. Cardiac neurosis, 700
- TOTH, LOUIS A. (*See* Byer, Ashman, and Toth), 796
- TRANCHESI, BERNARDINO. (*See* Decourt, Ramos, Jr., Tranchesi, Corea, Cavaleiro Dias, and Tisi), 697
- TWEED, PHYLLIS. (*See* Salans and Tweed), 477

U

- UNGERLEIDER, HARRY E., AND GUBNER, RICHARD. The Q_s and QS_s deflections in the electrocardiogram: criteria and significance, 807
- UTZ, DAVID C. (*See* Langley, Reed, and Utz), 730
- . (*See* Reed, Langley, and Utz), 701

V

- VACCAREZA, R. F., CROXATTO, LANARI, AND ALBERTI, V. J. Experimental stenosis of the pulmonary artery, 728
- VELEZ OROZCO, F. (*See* Sodi Pallares, Velez Orozco, and Rivero Carballo), 705
- VILLARREAL, HERNAN. (*See* Cortes and Villarreal), 715
- VIZCAINO, MARIO. (*See* Sodi Pallares, Vizcaino, Soberon, and Cabrera), 819

W

- WARBURG, ERIK. (*See* Hansen and Warburg), 709
- WARE, E. RICHMOND, AND CHAPMAN, BERNARD M. Chronic fibroplastic myocarditis, 530
- WEISBERGER, AUSTIN S., AND MACLAUGHLIN, JAMES A. Electrocardiographic changes associated with methyl alcohol poisoning, 27
- WEISMAN, S. A. Digitalis and quinidine in the treatment of auricular fibrillation, 719
- WERTENBERGER, GRACE E. (*See* Hafkesbring and Wertenberger), 84
- WHITE, PAUL D. (*See* Carlotti, Hardy, Jr., Linton, and White), 737
- WIGGERS, CARL J. Myocardial depression in shock: a survey of cardiodynamic studies, 633
- WILSON, FRANK N., JOHNSTON, FRANKLIN D., AND KOSSMANN, CHARLES E. The substitution of a tetrahedron for the Einthoven triangle, 594
- WINSOR, TRAVIS, ADOLPH, WILLIAM, RALSTON, WALTER C., AND LEIBY, GEORGE M. An objective clinical procedure for the determination of circulation velocity using fluorescent tracer substances, 704

Y

- YETTRA, M., AND LASKY, I. I. Aneurysmal dilatation of the aorta associated with cystic medial necrosis, 516

Z

- ZIMDAHL, WALTER T., AND KRAMER, LOUIS I. On the mechanism of paroxysmal tachycardia with rhythmic alternation in the direction of the ventricular complexes, 218
- ZODIKOFF, RUDOLPH. Multiple liver abscesses with rupture into the pericardium, 375

SUBJECT INDEX

A

- Abdominal aortography, retrograde, contribution to study of abdominal aorta and iliac arteries, 399*
- vena cava, effect of hemorrhage and shock on caliber of, 878*
- Abscesses, liver, multiple, with rupture into pericardium (Zodikoff), 375
- Acetylsalicylic acid, fate of, 130*
- Acidosis, tolerance of human heart to; reversible changes in RS-T interval during severe acidosis caused by administration of carbon dioxide (Altschule and Sulzbach), 458
- Acute coronary thrombosis, treatment of, with dicumarol (Nichol), 722
- edema of lungs and cardiac asthma in mitral stenosis with auricular fibrillation (Berconsky and Neuman), 738
- pulmonary edema, morphine treatment of (Gonzalez Sabathie), 738
- Adenosinetriphosphate, investigation of chemical changes in myocardial insufficiency with special reference to: cardiac muscle, 544*
- Age, effect of, on clinical effectiveness of nitroglycerin tablets, 401*
- Air embolism, pulmonary and arterial, differentiation of (Durant et al.), 269
- etiology of (Durant et al.), 271
- experimental, factors involved in fatality in (Durant et al.), 274
- (venous) (Durant et al.), 269
- Alcohol, methyl, poisoning, electrocardiographic changes associated with (Weisberger and MacLaughlin), 27
- Alternation, rhythmic, in direction of ventricular complexes, on mechanism of paroxysmal tachycardia with (Zimdahl and Kramer), 218
- Altitudes, high, natives of, physiologic condition of heart in (Rotta), 669
- American Heart Association, program of annual meeting and twentieth scientific meeting of, 742
- Amines, sympathomimetic, in heart muscle: pathogenic and therapeutic significance (Raab), 707
- Aminophylline, effect of, on prothrombin time in man, 549*
- trinitrin, and papaverine, action of certain drugs; importance of precordial leads in electrocardiograms after exertion in angina pectoris (Battro and Araya), 723
- Ammi visnaga* as coronary vasodilator, 128*
- in treatment of anginal syndrome, 128*
- Ammonium chloride, enteric coated, absorption of, 545*
- Amyloidosis, localized, resembling arteriosclerosis of heart, 547*
- systemic, primary, 392*
- Anastomoses, coronary, coronary arteriosclerosis, and myocardial infarction, 131*
- Anesthesia for sympathectomy in hypertension, 398*
- surgical, centennial of, annotated catalogue, 133 (B. Rev.)
- Aneurysm, arteriosclerotic, of cardiac coronary arteries (Mitchell), 112
- arteriovenous, of vertebral vessels, 543*
- dissecting, with hemopericardium (Ellis), 860
- of abdominal aorta, significance of calcification for roentgen diagnosis of, 887*
- Aneurysmal dilatation of aorta associated with cystic medial necrosis (Yettra and Lasky), 516
- Aneurysms and arteriovenous fistulae, arterial repair in treatment of, 553*
- Angina pectoris, anatomic data regarding surgical treatment of, 876*
- Cinnabane in treatment of, 548*
- importance of precordial leads in electrocardiograms after inertion in; action of certain drugs (trinitrin, aminophylline, and papaverine) (Battro and Araya), 723
- peptic, ulcer, and essential hypertension, relation of neurocirculatory dystonia to, 875*
- relationship to: hernia of esophageal hiatus (Nuzum), 724
- Anginal syndrome, *Ammi visnaga* in treatment of, 128*
- further observations on treatment of, with thiouracil (Ben-Asher), 490
- Angiocardiography, direct intracardiac (Chávez et al.), 560
- Angiography of aorta (Gomez del Campo and Meneses Hoyos), 729
- Angioscopy, retinal, in essential arterial hypertension (study of 300 clinical cases) (Puig Solanes), 733
- Annulus fibrosus, mitral, clinical aspects of calcification of, 885*
- Anoxemia, effect of pulmonary ventilation on, 395*
- Anterior poliomyelitis, acute, heart in (Geffer et al.), 228
- Anticoagulants, effect of, on postpartum bleeding, 405*
- Antigen-antibody reaction, influence of sodium salicylate on, 889*
- Antimony, effect of, on electrocardiogram, 554*
- Aorta, abdominal, significance of calcification for roentgen diagnosis of aneurysm of, 887*

An asterisk () after a page number indicates the reference is an abstract and not an original article.

- Aorta—Cont'd
aneurysmal dilatation* of, associated with cystic medial necrosis (Yettra and Lasky), 516
angiography of (Gomez del Campo and Meneses Hoyos), 729
coarctation of (Reifenstein et al.), 146
aortic stenosis, pulmonary stenosis, and patent ductus arteriosus, differential diagnosis of (Kerr), 725.
experimental medionecrosis of, 399*
human, cholesterol content of, in relation to serum cholesterol concentration, 888*
traumatic rupture of (Strassmann), 508
volume elasticity of, in intact dog (Katz et al.), 319
- Aortic arch anomalies, surgical significance of, 404*
double, and other anomalies of great vessels, roentgen diagnosis of, 129*
stenosis, pulmonary stenosis, patent ductus arteriosus, and coarctation of aorta, differential diagnosis of (Kerr), 725
- Aortography, abdominal, retrograde; contribution to study of abdominal aorta and iliac arteries, 399*
- Apex cardiogram and its utility in phonocardiography (Aixala), 703
- Argyrophil substance, basic, significance of, in pathogenesis of hypertension, 394*
- Army General Hospitals, diagnosis and treatment of thromboangiitis obliterans in vascular centers of (Freeman), 332
- Arrhythmias, benign residual (Gonzalez Sabathie and Gaspary), 729
cardiac, complicating total pneumonectomy, 879*
- Arterial blood, CO₂ tension in, and electrocardiogram in man, variations of, 879*
hypertension, essential retinal angioscopy in (study of 300 clinical cases) (Puig Solanes), 733
medical and surgical aspects (Martinez de la Cruz and Levy Boladeres), 733
pressure, action of urinary extracts of normal and hypertensive individuals and of hypertensive dogs upon, 391*
- Arteries, cardiac coronary, arteriosclerotic aneurysm of (Mitchell), 112
war wounds of, 265*
- Arterioles, retinal and choroidal in malignant hypertension: a clinical and pathologic study of fifteen cases, 885*
- Arteriosclerosis and ischemia, ulcer of leg due to, occurring in presence of hypertensive disease (hypertensive-ischemia ulcers), 266*
coronary, coronary anastomoses, and myocardial infarction, 131*
of heart, localized amyloidosis resembling, 547*
pulmonary, primary, relation to Ayerza's disease and; congenital dilatation of pulmonary arterial tree, 397*
- Arteriosclerotic aneurysm of cardiac coronary arteries (Mitchell), 112
- Arteriovenous fistula, aneurysms and, arterial repair in treatment of, 553*
effect of atropine on Branham sign in, 390*
roentgenologic kymographic studies of heart in presence of, and their interpretation, 550*
- Arteritis, temporal: report of case and comparison with respect to periarteritis nodosa, 555*
- Artery, coronary, disease, fatal, in young men (Poe), 76
left, origin of, from pulmonary artery (Kaunitz), 182
occlusion, acute, incidence of (Master), 135
single (Geever and Ravin), 538
pulmonary, experimental stenosis of (Vacarezza et al.), 728
origin of left coronary artery from (Kaunitz), 182
subclavian, role of clavicle in occlusion of, 124*
vein, and bone marrow, blood cultures made from, comparative study of, in patients with subacute bacterial endocarditis (Salazar Mallen et al.), 692
- Ascites, surgical treatment of, 401*
- Asthma, cardiac, and acute edema of lungs in mitral stenosis with auricular fibrillation (Berconsky and Neuman), 738
- Asystole, cardiac, in normal young man following physical effort (Eichna), 254
- Atabrine and electrocardiogram, 542*
protective action of, against chloroform-adrenaline ventricular fibrillation, 263
- Atherosclerosis and hypercholesterolemia, experimental and clinical studies in, and effect of decholesterolizing agents (Herrmann), 711
experimental; II. Effect of prolonged feeding of egg yolk powder in rats, 396*
- Atrionodal rhythm with ventricular bigeminy (Perelman and Miller), 34
- Atrioventricular excitation, anomalous sequence of ventricular stimulation and contraction in case of (Kossmann and Goldberg), 308
- Atropine, effect of, on Branham sign in arteriovenous fistula, 390*
- Auricular and ventricular beats, synchronization of, during complete heart block (Segers et al.), 685
complex, esophageal lead in study of, 881*
fibrillation and flutter, new drug for treatment of—fagarine (Taquini), 719
cardiac asthma, and acute edema of lungs in mitral stenosis with (Berconsky and Neuman), 738
demonstrated in infant of three months, progress report on case of, 544*
digitalis and quinidine in treatment of (Weisman), 719

Auricular—Cont'd

- flutter, influence of artificial obstacles on (II); flutter and fibrillation (Rosenblueth and Garcia Ramos), 677
- prefibrillation (Gonzalez Sabathie and Gaspary), 720
- right, and ventricular pressure in man, first recording of curves of, 127*
- tachycardia, paroxysmal, congestive heart failure and death in case of (Grant), 121

Auscultation, practical importance of, in first right intercostal space, 389*

A-V conduction, concealed: effect of blocked impulses on formation and conduction of subsequent impulses (Langendorf), 731

paraspecific conduction through upper connections of bundle of His-Tawara, Kent's fibers and (Mahaim), 651

Axis, medium, and ventricular gradient, easy method for calculating value of (Meneses Hoyos), 699

B

Bacterial endocarditis, acute, Lutembacher's syndrome complicated by (Geiger and Anderson), 240

treatment of, with penicillin, 880*

subacute, effect of anticoagulants on penicillin therapy and pathologic lesion of, 550*

experiences in treatment of, with penicillin (Greiger), 736

penicillin in treatment of: further studies in twenty-one patients (Jimenes Romo), 736

perforation of interventricular septum in case of (Levy, II, and Hull), 856

streptomycin in treatment of, 404*, 541*

Barium, effect of minute amounts of, on cardiac muscle, 396*

Benign residual arrhythmias (Gonzalez Sabathie and Gaspary), 729

Beriberi, acute, of nursing (2); cardiovascular manifestations of vitamin B deficiency in children of Cuba, 125*

Bigeminy, ventricular, atrionodal rhythm with (Perelman and Miller), 34

Bleeding, postpartum, effect of anticoagulants on, 405*

Blood, arterial, CO₂ tension in, and electrocardiogram in man, variations of, 879*

coagulation, changes in, following coronary thrombosis measured by heparin retarded clotting test (Waugh and Ruddick test), 409*

cultures made from artery, vein, and bone marrow, comparative study of, in patients with subacute bacterial endocarditis (Salazar Mallen et al.), 692

flow through forepaw during experimental shock, plethysmographic measurement of (Kondo et al.), 207

Blood—Cont'd

pressure, evaluation of certain drugs used to maintain, during spinal anesthesia, 264*

high, value of pressor test in (Taquini), 735

in hypertensive rats, influence of two thiourea derivatives on, 128*

levels of, in both arms and legs in normal subjects and patients suffering from certain disease, 884*

velocity of, relation between size of heart and (Meneely and Chesnut), 175

vessels, volume variations of large central, 879*

volume, relation of nitrogen balance and, to abnormalities of circulation (III); convalescence from surgical procedures, 541*

Boeck's sarcoid, electrocardiographic and spirometric findings in, 877*

Bone marrow, artery, and vein, blood cultures made from, comparative study of, in patients with subacute bacterial endocarditis (Salazar Mallen et al.), 692

Borderline case, so-called (1); cardiovascular manifestations of vitamin B deficiency in children of Cuba, 125*

Boston Lying-in Hospital, cardiac clinic of, report from, for first twenty-five years (Hamilton), 663

Botalli, patent ductus, in three sisters, 888*

Branham sign, effect of atropine on, in arteriovenous fistula, 390*

Bronchiectasis, dextrocardia and, 395*

Bundle branch block, localization of, electrocardiographic criteria and, 404*

review of 100 cases (Langley et al.), 730

of His-Tawara, upper connections of, Kent's fibers and A-V paraspecific conduction through (Mahaim), 651

C

Calcification, extensive in heart at early age, 888*

in mitral annulus fibrosus, clinical aspects of, 885*

significance of, for roentgen diagnosis of aneurysm of abdominal aorta, 887*

Carbon dioxide, reversible changes in RS-T interval during severe acidosis caused by administration of; tolerance of human heart to acidosis (Altschule and Sulzbach), 458

Cardiac action of Central American snake venom (Garcia Carillo), 709

arrhythmias complicating total pneumonectomy, 879*

asthma and acute edema of lungs in mitral stenosis with auricular fibrillation (Berconsky and Neuman), 738

asystole in normal young man following physical effort (Eichna et al.), 254

changes in malarial patients (Rojas and Deza), 702

Cardiac—Cont'd

- clinic of Boston Lying-in Hospital, report from, for first twenty-five years (Hamilton), 663
- coronary arteries, arteriosclerotic aneurysm of (Mitchell), 112
- enlargement, relation of, to hypertension in acute and chronic glomerulonephritis, 401*
- failure in tricuspid disease (Taquini), 727
- function in dog, effect of sulfonamide administration on (Hafkesbring and Wertenberger), 84
- hypertrophy so called idiopathic (4); cardiovascular manifestations of vitamin B deficiency in children of Cuba, 126*
- muscle, effect of minute amounts of barium on, 396*
 - further studies: investigation of chemical changes in myocardial insufficiency with special reference to adenosine-triphosphate, 544*
 - influence of G-strophanthin on mechanical properties of, 396*
- neurosis (Toro Villa), 700
- pain (Sutton), 724
- silhouette, determination of frontal plane area from product of long and short diameters of, 400*
- sound, first, in premature contractions (Cosio), 707
- symptoms, functional, in 50-year-old men, consideration of pathogenesis and treatment of, 389*
- Cardiodynamic studies, survey of; myocardial depression in shock (Wiggers), 633
- Cardiogram, apex, and its utility in phonocardiography (Aixala), 703
- Cardiology, Second Inter-American Congress of, and formation of Inter-American Society of Cardiology, 557
- Cardiovascular actions of 2,3-dimercaptopanols (BAL), 390*
 - changes due to insulin, mechanism and prevention of, 889*
 - disorders, studies on nature of certain symptoms associated with, 553*
 - manifestations of vitamin B deficiency in children of Cuba; 1. So-called borderline case, 125*
 - 2. Acute beriberi of nursing, 125*
 - 3. Pellagra - beriberi syndrome, 126*
 - 4. So-called idiopathic cardiac hypertrophy, 126*
- patients who do not present a frank syndrome of avitaminosis or of hypovitaminosis but are nevertheless clinically improved by administration of this vitamin (B₁), amount of vitamin B₁ in urine of, 544*
- sounds and murmurs, writing symbols to describe, while listening (Segall), 705
- syphilis, treatment of, with penicillin, 555*
- Carditis, acute rheumatic, in children, duration of electrical systole (Q-T) in (Taran and Szilagyi), 14
- Carotid sinus reflex, hyperactive, attacks of unconsciousness resulting from (Smith), 711
- Catheterization, heart, in man, endocardiac electrocardiogram obtained by (Battro and Bidoggia), 604
- Cava, vena, abdominal, effect of hemorrhage and shock on caliber of, 878*
- Cell, liver, alterations in structure of, in congestive heart failure (Costero and Barroso-Moguel), 701
- Centennial of surgical anesthesia, annotated catalogue, 133 (B. Rev.)
- Central American snake venom, cardiac action of (Garcia Carillo), 709
 - blood vessels, large, volume variations of, 879*
- Cerebral and peripheral emboli, study of, registered in National Institute of Cardiology of Mexico (Mendez Hernandez), 712
 - vascular occlusions in young adults, 391*
- Chagas' disease, chronic heart involvement in (Decourt et al.), 697
- Chest films, routine, heart size from, 400*
- Children, duration of electrical systole (Q-T) in acute rheumatic carditis in (Taran and Szilagyi), 14
 - precordial leads in, 130*
- Chile, heart disease in, medical-social feature of (Herve), 710
- Chloroform-adrenaline ventricular fibrillation, protective action of atrabine against, 263*
- Cholesterol concentration, serum, cholesterol content of human aorta in relation to, 888*
 - content of human aorta in relation to serum cholesterol concentration, 888*
 - levels in various diseases and effects of decholesterizing agents, 263*
- Chordotomy, cervical, high, painful phantom limb treated by, 393*
- Choroidal and retinal arterioles in malignant hypertension: a clinical and pathologic study of fifteen cases, 885*
- Chronic heart involvement in Chagas' disease (Decourt et al.), 697
- Cinnabane in treatment of anigna pectoris, 548*
- Circulation, coronary, post mortem, preliminary study of (Salans and Tweed), 477
 - studies on; II. Collateral circulation of normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres (Prinzmetal et al.), 420
 - pulmonary, observations on volume of, and its importance in production of cyanosis and polycythemia (Tausig and Blalock), 413
 - systemic, in man, observations on dynamics of, 881*

- Circulation—Cont'd
 time, influence of heart size on (Nathanson and Elek), 464
 velocity, objective clinical procedure for determination of, using fluorescent tracer substances (Winsor et al.), 704
- Circulatory changes resulting from obstetric labor (Sampson et al.), 703
 collapse, kidney functions and; post-syncopal oliguria, 408*
- diseases; nordisk laerebog i intern medicin vol. IV, 410 (B. Rev.)
 system, effects of quinidine on, 542*
- Clavicle, role of, in occlusion of subclavian artery, 124*
- Clinical and radiologic examinations, comparative studies with three types of electrocardiographic leads (classic, unipolar extremity leads, and multiple precordial leads) in relation to (Ramos et al.), 699
 procedure, objective, for determination of circulation velocity using fluorescent tracer substances (Winsor et al.), 704
- Closure of interauricular septal defects in dogs, experimental method for (Cohn), 453
- CO₂ tension in arterial blood and electrocardiogram in man, variations of, 879*
- Coarctation of aorta (Reifenstein et al.), 146
 aortic stenosis, pulmonary stenosis, and patent ductus arteriosus, differential diagnosis of (Kerr), 725
- Collateral circulation in extremities, tests for, 551*
 of normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres (II); studies on coronary circulation (Prinzmetal et al.), 420
- Complex, auricular, esophageal lead in study of, 881*
- Complexes, ventricular, on mechanism of paroxysmal tachycardia with rhythmic alternation in direction of (Zimdahl and Kramer), 218
- Concentration of renin in renal venous blood in patients with chronic heart failure, 878*
- Conduction, concealed A-V; effect of blocked impulses on formation and conduction of subsequent impulses (Langendorf), 731
- Congenital heart diseases, classification of (de los Reyes and Castellanos), 727
 paroxysmal tachycardia (Garvin and Kline), 362
- Congestive heart failure, alterations in structure of liver cell in (Costero and Barroso-Moguel), 701
 and death in case of paroxysmal auricular tachycardia (Grant), 121
 treatment of (Cooley), 740
- Congress of Cardiology, Second Inter-American, and formation of Inter-American Society of Cardiology, 557
- Contraction, ventricular stimulation and, sequence of, in case of anomalous atrioventricular excitation (Kossmann and Goldberg), 308
- Contractions, premature, first cardiac sound in (Cossio), 707
- Coronary arteries, cardiac, arteriosclerotic aneurysm of (Mitchell), 112
 arteriosclerosis, coronary anastomoses, and myocardial infarction, 131*
 artery disease, fatal, in young men (Poe), 76
 prevalence of (Master), 135
 left, origin of, from pulmonary artery (Kaunitz), 182
 occlusion, acute, incidence of (Master), 135
 prevalence of (Master), 136
 single (Geever and Ravin), 538
 circulation post mortem, preliminary study of (Salans and Tweed), 477
 studies on; II. Collateral circulation of normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres (Prinzmetal et al.), 420
 diseases, increase in (Master), 137
 perfusion with radioactive erythrocytes and glass spheres, collateral circulation of normal human heart by (II); studies on coronary circulation (Prinzmetal et al.), 420
 thrombosis, acute, treatment of, with dicumarol (Nichol), 722
 changes in blood coagulation following, measured by heparin retarded clotting test (Waugh and Ruddick test), 409*
 vasodilator, *Amni visnaga* as, 128*
- Cortical excisions for relief of intractable pain in extremities, experiences with, 543*
- Cyanosis and polycythemia, observations on volume of pulmonary circulation and its importance in production of (Taussig and Blalock), 413
- Cystic medial necrosis, aneurysmal dilatation of aorta associated with (Yettra and Lasky), 516
- D
- Damage, myocardial, in starvation, 877*
- Death, congestive heart failure and, in case of paroxysmal auricular tachycardia (Grant), 121
 sudden and unexpected, of young soldiers, 882*
- Decholesterolizing agents, cholesterol levels in various diseases and, 263*
 effect of, experimental and clinical studies in hypercholesterolemia and atherosclerosis and (Herrmann), 711
- Decompensation, weight of red blood corpuscles in heart failure determined with labelled erythrocytes during and after (Nylin and Hedlund), 770

- Deficiency, vitamin E, electrocardiogram of rats on, 881*
- Deflection, intrinsic, in normal cases and in ventricular hypertrophy, 886*
- QRS, abnormally small, in one or more precordial leads, significance of (Lapin), 747
- Depression, myocardial, in shock (Wiggers), 633
- Dextrocardia and bronchiectasis, 395*
- (isolated dextrocardia with inversion of chambers), considerations on rare case of, 390*
- Diagnostic value of electrocardiographic patterns based on assay of 261 additional autopsied cases (Katz et al.), 696
- Dicumarol, treatment of acute coronary thrombosis with (Nichol), 722
- Digitalis and ouabain, action of, on certain properties of myocardium, 387*
- and quinidine in treatment of auricular fibrillation (Weisman), 719
- effect, mechanism of, significance of ventricular oxygen consumption and enzymatic liberation of phosphorus in (Guerra), 705
- Dilatation, aneurysmal, of aorta associated with cystic medial necrosis (Yettra and Lasky), 516
- 2,3-Dimercaptopropanol (BAL), cardiovascular actions of, 390*
- Disease, Chagas', chronic heart involvement in (Decourt et al.), 697
- Dissecting aneurysm with hemopericardium (Ellis), 860
- Diuretics, mercurial, on toxicity of: observations on eighteen cases with suggestions for prevention of toxic reaction, 548*
- Ductus arteriosus, patent, results of surgery in (Shapiro and Johnson), 725
- patent, Botalli, in three sisters, 888*
- Dynamics of systemic circulation in man, observations on, 881*
- Dystonia, neurocirculatory, relation of, to essential hypertension, angina pectoris, and peptic ulcer, 875*
- E
- Ebstein type, tricuspid insufficiency of, report of case of, with probable fetal endocarditis and exceptional electrocardiographic characteristics (Berber), 726
- Edema, acute, of lungs, and cardiac asthma in mitral stenosis with auricular fibrillation (Berconsky and Neuman), 738
- pulmonary, morphine treatment of (Gonzalez Sabathie), 738
- in pregnant patient with mitral stenosis (Peters and Penner), 528
- Effort, injury and, effect of, on normal and diseased heart, 552*
- physical, cardiac asystole in normal young man following (Eichna et al.), 254
- Egg yolk powder, effect of prolonged feeding of, in rats (II); experimental atherosclerosis, 396*
- Egypt, bilharzial heart disease in, 409*
- Einthoven triangle, substitution of tetrahedron for (Wilson et al.), 594
- Elasticity, volume, of aorta in intact dog (Katz et al.), 319
- Electric manometer, improved, for measuring intra-arterial, intravenous, and intracardial pressure, with general theory of manometers (Hansen and Warburg), 709
- Electrical systole (Q-T), duration of, in acute rheumatic carditis in children (Taran and Szilagyi), 14
- Electrocardiogram and CO₂ tension in arterial blood in man, variations of, 879*
- atrabrine and, 542*
- effect of antimony on, 554*
- endocardiac, obtained by heart catheterization in man (Battro and Bidoggia), 604
- importance of precordial leads in, after exertion in angina pectoris; action of certain drugs (trinitrin, aminophylline, and papaverine) (Battro and Araya), 723
- monophasic, of ventricle, various components of, 885*
- of older pilots, 129*
- of rats on vitamin E deficiency, 881*
- precordial, influence of nonindifferent electrode upon, 391*
- Q_s and QS₃ deflections in: criteria and significance (Ungerleider and Gubner), 807
- significance of concordant inverted initial ventricular deflections in, of patients with pulmonary tuberculosis, 402*
- with large, upright T waves and long Q-T intervals (Byer et al.), 796
- Electrocardiograph, simultaneous, of mother, congenital complete heart block diagnosed in utero with sound tracings and (Jordan and Randolph), 109
- Electrocardiographic abnormalities in severe malnutrition, 403*
- and spirometric findings in Boeck's sarcoid, 877*
- changes associated with methyl alcohol poisoning (Weisberger and MacLaughlin), 27
- characteristics, exceptional, and probable fetal endocarditis, report of case of tricuspid insufficiency of Ebstein type with (Berber), 726
- criteria and localization of bundle branch block, 404*
- effects of prostigmine, 549*
- features of myocardial infarction as affected by involvement of septum and by complete and incomplete transmural involvement, 401*
- findings in patients with peptic ulcers, 397*

Electrocardiographic—Cont'd

- leads (classic, unipolar extremity leads, and multiple precordial leads), comparative studies with three types of, in relation to clinical and radiologic examinations (Ramos et al.), 699
- patterns, diagnostic value of, based on assay of 261 additional autopsied cases (Katz et al.), 696
- phenomena associated with spontaneous pneumothorax and mediastinal emphysema, 884*
- studies in Puerto Rico with unipolar precordial leads in normal individuals of both sexes and at different ages (Suarez), 731
- in rheumatic heart disease with reference to interpretation of multiple unipolar precordial leads (First et al.), 1
- study of psychoneurotic patients, 553*
- Electrocardiography, direct, of heart during restoration (resuscitation of isolated human heart), 547*
- in hypertension; study of patients subjected to lumbodorsal splanchnicectomy, 388*
- Emboli, cerebral and peripheral, study of, registered in National Institute of Cardiology of Mexico (Mendez Hernandez), 712
- Embolism, pulmonary, in medical patients: comparison of incidence, diagnosis, and effects of treatment of 273 cases at Massachusetts General Hospital in two five-year periods (Carloti et al.), 737
- (venous) air (Durant et al.), 269
- Emphysema, mediastinal, acute, 546*
- and spontaneous pneumothorax, electrocardiographic phenomena associated with, 884*
- spontaneous, with acute right ventricular strain (Klein), 867
- Employment, competitive, selective placement of patients with heart disease in (Kossmann et al.), 700
- Encephalopathy of rheumatic patient (de Gortari et al.), 716
- rheumatic, 887*
- Endocardiac electrocardiogram obtained by heart catheterization in man (Battro and Bidoggia), 604
- Endocarditis, acute bacterial, treatment of, with penicillin, 880*
- bacterial, acute, Lutembacher's syndrome complicated by (Geiger and Anderson), 240
- experimental, of dogs, 405*
- probable fetal, and exceptional electrocardiographic characteristics, report of case of tricuspid insufficiency of Ebstein type with (Berber), 726
- rheumatic valvular, clinical features of 1,160 cases of (Cortes and Villarreal), 715

Endocarditis—Cont'd

- subacute bacterial, comparative study of blood cultures made from artery, vein, and bone marrow in patients with (Salazar Mallen et al.), 692
 - experiences in treatment of, with penicillin (Greiger), 736
 - penicillin in treatment of: further studies in twenty-one patients (Jimenes Romo), 736
 - perforation of interventricular septum in (Levy, II, and Hull), 856
 - Enzymatic liberation of phosphorus and ventricular oxygen consumption, significance of, in mechanism of digitalis effect (Guerra), 705
 - Epinephrine, case of large overdose of (Horwitz), 107
 - effect on heart of overdose of (McGinty and Baer), 102
 - Erythrocytes, labelled, weight of red blood corpuscles in heart failure determined with, during and after decompensation (Nylin and Hedlund), 770
 - radioactive, and glass spheres, collateral circulation of normal human heart by coronary perfusion with (II); studies on coronary circulation (Prinzmetal et al.), 420
 - Esophageal-hiatus, hernia of: relationship to angina pectoris (Nuzum), 724
 - Esophageal lead in study of auricular complex, 881*
 - Ethyl alcohol, 95 per cent, oral administration of, or substantial meal, effect of smoking on vasodilatation produced by (Roth and Sheard), 654
 - Excitation, anomalous atrioventricular, sequence of ventricular stimulation and contraction in case of (Kossmann and Goldberg), 308
 - Exercise, nitrites and, effect of, on inverted T wave, 402*
 - Experimental hypertension in dog, 881*
 - method for closure of interauricular septal defects in dogs (Cohn), 453
 - shock, plethysmographic measurement of blood flow through forepaw during (Kondo et al.), 207
- F
- Fagarine—new drug for treatment of auricular fibrillation and flutter (Taquini), 719
 - Failure, cardiac, in tricuspid disease (Taquini), 727
 - congestive heart, alterations in structure of liver cell in (Costero and Barros-Moguel), 701
 - treatment of (Cooley), 740
 - Fallot, tetralogy of (Middleton and Ritchie), 250
 - Fetal endocarditis, probable, and exceptional electrocardiographic characteristics, report of case of tricuspid insufficiency of Ebstein type with (Berber), 726

- Fever, rheumatic, incidence and clinical features of, in Mexico City (Robles Gil), 713
 is orthodox therapy of, conducive to psychosomatic disability? (Adamson), 715
- Fibrillation and flutter; II. Influence of artificial obstacles on experimental auricular flutter (Rosenblueth and Garcia Ramos), 677
 auricular, and flutter, new drug for treatment of—fagarine (Taquini), 719
 cardiac asthma and acute edema of lungs in mitral stenosis with (Berconsky and Neuman), 738
 digitalis and quinidine in treatment of (Weisman), 719
- Fibroplastic myocarditis, chronic (Ware and Chapman), 530
- Fibrosis, annulus, mitral, clinical aspects of calcification of, 885*
- Fluorescent tracer substances, objective clinical procedure for determination of circulation velocity using (Winsor et al.), 704
- Flutter and auricular fibrillation, new drug for treatment of—fagarine (Taquini), 719
 and fibrillation; II. Influence of artificial obstacles on experimental auricular flutter (Rosenblueth and Garcia Ramos), 677
- Forepaw, plethysmographic measurement of blood flow through, during experimental shock (Kondo et al.), 207
- Frontal plane area, determination of, from product of long and short diameters of cardiac silhouette, 400*
- Fusion beats, different mechanisms of (Malinow and Langendorf), 705
- G
- Gangrene, surgical treatment of, in trench foot, 406*
- Glass spheres, collateral circulation of normal human heart by coronary perfusion with radioactive erythrocytes and (II); studies on coronary circulation (Prinzmetal et al.), 420
- Glomerulonephritis, acute and chronic, relation of cardiac enlargement to hypertension in, 401*
- Gradient, ventricular, and medium axis, easy method for calculating value of (Meneses Hoyos), 699
- Great vessels, roentgen diagnosis of double aortic arch and other anomalies of, 129*
- G-strophanthin, influence of, on mechanical properties of cardiac muscle, 396*
 lethal dose and average rate of uptake of, in heart-lung preparation of dog under varying conditions, 264*
- H
- Heart, action of magnesium on, 403*
 block, complete, in pregnancy (report of two successful deliveries), 545*
- Heart block—Cont'd
 synchronization of auricular and ventricular beats during (Segers et al.), 685
 congenital complete, diagnosed in utero with sound tracings and simultaneous electrocardiograph of mother (Jordan and Randolph), 109
 postural, 542*
 catheterization in man, endocardial electrocardiogram obtained by (Battro and Bidoggia), 604
 clinical roentgenology of, 410 (B. Rev.)
 death, sudden, pathological anatomy of, 397*
 diffuse, scleroderma with involvement of (Mathisen and Palmer), 366
 disease and pregnancy (Laubry and Routier), 739
 bilharzial, in Egypt, 409*
 congenital, classification of (de los Reyes and Castellanos), 727
 in children in rural town country; particularly in relation to rheumatic fever, 888*
 in Chile, medical-social features of (Herve), 710
 organic, study of abnormal T waves in patients presenting no evidence of, 546*
 rheumatic, electrocardiographic studies in, with reference to interpretation of multiple unipolar precordial leads (First et al.), 1
 selective placement of patients with, in competitive employment (Kossmann et al.), 700
 effect on, of overdose of epinephrine (McGinty and Baer), 102
 extensive calcification in, at early age, 888*
 failure, chronic, concentration of renin in renal venous blood in patients with, 878*
 congestive, alterations in structure of liver cell in (Costero and Barroso-Moguel), 701
 and death in case of paroxysmal auricular tachycardia (Grant), 121
 preponderance of right hydrothorax in, 555*
 treatment of (Cooley), 740
 low output, effects of venesection in, 878*
 weight of red blood corpuscles in, determined with labelled erythrocytes during and after decompensation (Nylin and Hedlund), 770
- foreign bodies in and in relation to thoracic blood vessels and, 124*
- human, normal, collateral circulation of, by coronary perfusion with radioactive erythrocytes and glass spheres (II); studies on coronary circulation (Prinzmetal et al.), 420
 tolerance of, to acidosis; reversible changes in RS-T interval during severe acidosis caused by administration of carbon dioxide (Altschule and Sulzbach), 458

Heart—Cont'd

- in acute anterior poliomyelitis (Geftter et al.), 228
- in sternal depression, 403*
- in uremia (Langendorf and Pirani), 282
- influence of vitamin B₁ deficiency on pyruvate exchange of (Randles et al.), 341
- involvement, chronic, in Chagas' disease (Decourt et al.), 697
- lung preparation of dog, lethal dose and average rate of uptake of g-strophanthin in, under varying conditions, 264*
- muscle, note on pentose isolated from (Sodi Pallares et al.), 705
 - sympathomimetic amines in: pathogenic and therapeutic significance (Raab), 707
- normal and diseased, effect of injury and effort on, 552*
- physiologic condition of, in natives of high altitudes (Rotta), 669
- size from routine chest films, 400*
 - influence of, on circulation time (Nathanson and Elek), 464
 - of, and velocity of blood, relation between (Meneely and Chesnut), 175
- sound in mitral stenosis, studies on (Meneses Hoyos et al.), 706
- Hemangiomas, skin, vascular tumours of spinal cord associated with, 393*
- Hemoglobin and total plasma protein, changes in, after injection of mercurophylline, 387*
- Hemopericardium, dissecting aneurysm with (Ellis), 860
- Hemorrhage and shock, effect of, on caliber of abdominal vena cava, 878*
- Heparin retarded clotting test (Vaugh and Ruddick test), changes in blood coagulation following coronary thrombosis measured by, 409*
 - use of, in retarding menstruum, effects and drawbacks in, 875*
- Hernia of esophageal hiatus: relationship to angina pectoris (Nuzum), 724
- His-Tawara, bundle of, Kent's fibers and A-V paraspecific conduction through upper connections of (Mahaim), 651
- Human heart, normal, collateral circulation of, by coronary perfusion with radioactive erythrocytes and glass spheres (II); studies on coronary circulation (Prinzmetal et al.), 420
 - tolerance of, to acidosis; reversible changes in RS-T interval during severe acidosis caused by administration of carbon dioxide (Altschule and Sulzbach), 458
- Hydrothorax, right, preponderance of, in congestive heart failure, 555*
- Hypercholesterolemia and atherosclerosis, experimental and clinical studies in, and effect of decholesterolizing agents (Herrmann), 711

- Hypertension, anesthesia for sympathectomy in, 398*
 - arterial—medical and surgical aspects (Martinez de la Cruz and Levy Bolad-eres), 733
 - electrocardiography in; study of patients subjected to lumbodorsal splanchnicectomy, 388*
 - essential, angina pectoris, and peptic ulcer, relation of neurocirculatory dystonia to, 875*
 - arterial, retinal angiography in (Puig Solanes), 733
 - experimental, in dog, 881*
 - in dog, hypertension in cow, and pepsin, conclusions based upon experiments with, 889*
 - influence of steroids on restoration of, in hypophysectomized rats, 881*
 - malignant, retinal and choroidal arterioles in: a clinical and pathologic study of fifteen cases, 885*
 - pathogenesis and treatment of (Grollman), 721
 - relation of cardiac enlargement to, in acute and chronic glomerulonephritis, 401*
 - renal, 132 (B. Rev.)
 - role of surgical treatment in management of (Peet and Isberg), 735
 - significance of basic argyrophil substance in pathogenesis of, 394*
 - surgical approach to, 266*
- Hypertensive disease, ulcer of leg due to arteriosclerosis and ischemia, occurring in presence of, (hypertensive-ischemia ulcers), 266*
- rats, influence of two thiourea derivatives on blood pressure in, 128*
- Hypertrophy, ventricular, intrinsic deflection in normal cases and in, 886*
- Hypophysectomized rats, influence of steroids on restoration of hypertension in, 881*

I

- Impulses, blocked, effect of, on formation and conduction of subsequent impulses; concealed A-V conduction (Langendorf), 731
- In memoriam—Cesare Pezzi, 386
 - Carl J. Rothberger, 385
- Incidence of acute coronary artery occlusion (Master), 135
- Infant of three months, progress report on case of auricular fibrillation demonstrated in, 544*
- Infarction, comparison between leads from extremities, precordial leads CF₂ and IV F, and Nehb's leads, with special regard to diagnosis of, 888*
 - myocardial, acute, 407*
 - incidence of thrombo-embolic lesions accompanying (Hellerstein and Martin), 443
 - treatment of shock accompanying (Schwartz), 169

- Infarcts, myocardial, critical examination of current classification of localization of (author's terminology) (Bosco), 722
- Inflammatory processes, other, and rheumatic disease, significance of interstitial lymphocytosis in (Costero), 717
- Injury and effort, effect of, on normal and diseased heart, 552*
- Insufficiency, tricuspid, new diagnostic sign of (Rivero Carvallo), 728
sign of, 881*
- Insulin, cardiovascular changes due to, mechanism and prevention, 889*
- Inter-American Congress, Second, of Cardiology and formation of Inter-American Society of Cardiology, 557
- Interauricular septal defects in dogs, experimental method for closure of (Cohn), 453
- Intercostal space, first right, practical importance of auscultation in, 389*
- Intern medicin, nordisk laerebog i, vol. IV; circulatory diseases, 410 (B. Rev.)
- Interstitial lymphocytosis, significance of, in rheumatic disease and in other inflammatory processes (Costero), 717
- Interventricular septum, perforation of, in case of subacute bacterial endocarditis (Levy, II, and Hull), 856
- Intra-arterial, intravenous, and intracardial pressure, improved electric manometer for measuring, with general theory of manometers (Hansen and Warburg), 709
- Intracardiac angiocardiology, direct (Chávez et al.), 560
- Intracardial, intra-arterial, and intravenous pressure, improved electric manometer for measuring, with general theory of manometers (Hansen and Warburg), 709
- Intracavity potential in man and dog, comparative study of (Sodi Pallares et al.), 819
- Intractable pain in extremities, experiences with cortical excisions for relief of, 543*
- Intravenous, intra-arterial, and intracardial pressure, improved electric manometer for measuring, with general theory of manometers (Hansen and Warburg), 709
- Intrinsic deflection in normal cases and in ventricular hypertrophy, 886*
- Ischemia, ulcer of leg due to arteriosclerosis and, occurring in presence of hypertensive disease (hypertensive-ischemia ulcers), 266*

K

- Kent's fibers and A-V paraspecific conduction through upper connections of bundle of His-Tawara (Mahaim), 651
- Kidney function and circulatory collapse; post-syncope oliguria, 408*

L

- Labelled erythrocytes, weight of red blood corpuscles in heart failure determined with, during and after decompensation (Nylin and Hedlund), 770
- Labor, obstetric, circulatory changes resulting from (Sampson et al.), 703
- Lead, esophageal, in study of auricular complex, 881*
- Leads CF₂ and IV F, precordial, Nehb's leads, and leads from extremities, comparison between, with special regard to diagnosis of infarction, 888*
- different precordial, comparative study of (Meneses Hoyos and Gonzalez Tomayo), 698
- electrocardiographic (classic, unipolar extremity leads, and multiple precordial leads), comparative studies with three types of, in relation to clinical and radiologic examinations (Ramos et al.), 699
- from extremities, precordial leads CF₂ and IV F, and Nehb's leads, comparison between, with special regard to diagnosis of infarction, 888*
- multiple precordial, review of eight cases of Wolff-Parkinson-White syndrome including four cases with initial left ventricular activation as demonstrated by (Reed et al.), 701
- unipolar precordial, electrocardiographic studies in rheumatic heart disease with reference to interpretation of (First et al.), 1
- precordial, importance of, in electrocardiograms after exertion in angina pectoris; action of certain drugs (trinitrin, aminophylline, and papaverine) (Battro and Araya), 723
- significance of abnormally small QRS deflections in one or more (Lapin), 747
- unipolar precordial, in normal individuals of both sexes and at different ages, electrocardiographic studies in Puerto Rico with (Suarez), 731
- Lesions, thrombo-embolic, accompanying myocardial infarction, incidence of (Hallerstein and Martin), 443
- Liver abscesses, multiple, with rupture into pericardium (Zodikoff), 375
- cell, alterations in structure of, in congestive heart failure (Costero and Barroso-Moguel), 701
- Lumbodorsal splanchnicectomy, study of patients subjected to; electrocardiography in hypertension, 388*
- Lungs, acute edema of, and cardiac asthma, in mitral stenosis with auricular fibrillation (Berconsky and Neuman), 738
- Lutembacher's syndrome complicated by acute bacterial endocarditis (Geiger and Anderson), 240

- Lymphocytosis, interstitial, significance of, in rheumatic disease and in other inflammatory processes (Costero), 717
- M
- Magnesium, action of, on heart, 403*
- Malarial patients, cardiac changes in (Rojas and Deza), 702
- Malignant hypertension, retinal and choroidal arterioles in malignant hypertension: a clinical and pathologic study of fifteen cases, 885*
- Malnutrition, severe, electrocardiographic abnormalities in, 403*
- Manometer, improved, electric, for measuring intra-arterial, intravenous, and intracardial pressure, with general theory of manometers (Hansen and Warburg), 709
- Massachusetts General Hospital, comparison of incidence, diagnosis, and effects of treatment of 273 cases at, in two five-year periods: pulmonary embolism in medical patients (Carloti et al.), 737
- Meal, substantial, or 95 per cent ethyl alcohol, oral administration of, effect of smoking on vasodilatation produced by (Roth and Sheard), 654
- Mechanisms, different, of fusion beats (Malinow and Langendorf), 705
- Medial necrosis, cystic, aneurysmal dilatation of aorta associated with (Yettra and Lasky), 516
- Mediastinal emphysema, acute, 546*
spontaneous, with acute right ventricular strain (Klein), 867
- Medical management of peripheral vascular disorders, 392*
- Medical-social features of heart disease in Chile (Herve), 710
- Medionecrosis, experimental, of aorta, 399*
- Medium axis and ventricular gradient, easy method for calculating value of (Meneses Hoyos), 699
- Memoir on new use of sulfuric ether, 133 (B. Rev.)
- Men, Raynaud's disease in (Abramson and Shumacker), 500
young, fatal coronary artery disease in (Poe), 76
- Menstruum, effects and drawbacks in use of heparin in retarding, 875*
- Mercurial diuretics, on toxicity of: observations on eighteen cases with suggestions for prevention of toxic reaction, 548*
poisoning, fatal, following prolonged administration of mercurophylline, 394*
preservatives, venous thrombosis after infusion with gelatin solutions containing, 542*
- Mercurophylline, changes in hemoglobin and total plasma protein after injection of, 387*
fatal mercurial poisoning following prolonged administration of, 394*
- Methyl alcohol poisoning, electrocardiographic changes associated with (Weisberger and MacLaughlin), 27
- Mexico City, incidence and clinical features of rheumatic fever in (Robles Gil), 713
National Institute of Cardiology of, study of cerebral and peripheral emboli, registered in (Mendez Hernandez), 712
- Micro-nodulation, manifestation of pulmonary stasis in presence of mitral disease, 389*
- Mitral annulus fibrosus, clinical aspects of calcification of, 885*
stenosis, pulmonary edema in pregnant patient with (Peters and Penner), 528
studies on heart sound in (Meneses Hoyos et al.), 706
with auricular fibrillation, cardiac asthma and acute edema of lungs in (Bercovsky and Neuman), 738
valve, pathology, of, in older age groups (Rosenthal and Feigin), 346
- Monophasic electrocardiogram of ventricle, various components of, 885*
- Morphine, intravenous use of, in treatment of paroxysmal ventricular tachycardia (Gonzalez Sabathie), 719
treatment of acute pulmonary edema (Gonzalez Sabathie), 738
- Murmurs and cardiovascular sounds, writing symbols to describe, while listening (Segall), 705
- Muscle, heart, note on pentose isolated from (Sodi Pallares et al.), 705
sympathomimetic amines in: pathogenic and therapeutic significance (Raab), 707
- Myocardial changes following sulfonamides, 392*
damage in starvation, 877*
depression in shock (Wiggers), 633
infarction, acute, 407*
coronary arteriosclerosis, coronary anastomoses, and, 131*
electrocardiographic features of, as affected by involvement of septum and by complete and incomplete transmural involvement, 401*
incidence of thrombo-embolic lesions accompanying (Hellerstein and Martin), 443
treatment of shock accompanying (Schwartz), 169
infarcts, critical examination of current classification of localization of (author's terminology) (Bosco), 722
insufficiency, investigation of chemical changes in, with special reference to adenosinetriphosphate: cardiac muscle, 544*
- Myocarditis, fibroplastic, chronic (Ware and Chapman), 530
- Myocardium, action of digitalis and ouabain on certain properties of, 387*

N

- Naval enlisted personnel, rheumatic fever in;
II. Effectiveness of intensive salicylate therapy in cases of acute infection, 388*
- personnel, indications and results of surgery of autonomic nervous system in, 265*
- Necrosis, medial, cystic, aneurysmal dilatation of aorta associated with (Yettra and Lasky), 516
- Negro, male, untreated syphilis in: evidence of cardiovascular abnormalities and other forms of morbidity, 882*
- thromboangiitis obliterans in (Breidenbach, Jr., and Palmer), 849
- Nehb's leads, leads from extremities, and precordial Leads CF₂ and IV F, comparison between, with special regard to diagnosis of infarction, 888*
- Nervous system, autonomic, indications and results of surgery of, in Naval personnel, 265*
- Neurocirculatory dystonia, relation of, to essential hypertension, angina pectoris, and peptic ulcer, 875*
- Neurosis, cardiac (Toro Villa), 700
- Nitrites and exercise, effect of, on inverted T wave, 402*
- Nitrogen balance and blood volume, relation of, to abnormalities of circulation (III); convalescence from surgical procedures, 541*
- Nitroglycerin tablets, effect of age on clinical effectiveness of, 401*
- Normal young man, cardiac asystole in, following physical effort (Eichna et al.), 254

O

- Obliterans, thromboangiitis, clinical impression of therapy in (McGovern), 712
- in Negro (Breidenbach, Jr., and Palmer), 849
- Obstacles, artificial, influence of, on experimental auricular flutter (II); flutter and fibrillation (Rosenbluth and Garcia Ramos), 677
- Obstetric labor, circulatory changes resulting from (Sampson et al.), 703
- Occlusion, acute coronary artery, incidence of (Master), 135
- Occlusions, vascular, cerebral, in young adults, 391*
- Older age groups, pathology of mitral valve in (Rosenthal and Feigin), 346
- Ouabain, digitalis and, action of, on certain properties of myocardium, 387*
- Overdose, large, of epinephrine, case of (Horwitz), 107
- of epinephrine, effect on heart of (McGinty and Baer), 102
- Oxygen consumption, ventricular, and enzymatic liberation of phosphorus, significance of, in mechanism of digitalis effect (Guerra), 705

P

- Pain, cardiac (Sutton), 724
- victory over, 132 (B. Rev.)
- Papaverine, trinitrin, and aminophylline, action of certain drugs; importance of precordial leads in electrocardiograms after exertion in angina pectoris (Battro and Araya), 723
- Paroxysmal auricular tachycardia, congestive heart failure and death in case of (Grant), 121
- tachycardia, congenital (Garvin and Kline), 362
- transitory flutter and fibrillation, 884*
- with rhythmic alteration in direction of ventricular complexes, on mechanism of (Zimdahl and Kramer), 218
- with syncope, 391*
- ventricular tachycardia, intravenous use of morphine in treatment of (Gonzalez Sabathie), 719
- Patent ductus arteriosus, aortic stenosis, pulmonary stenosis, and coarctation of aorta, differential diagnosis of (Kerr), 725
- results of surgery in (Shapiro and Johnson), 725
- Botalli in three sisters, 888*
- Pathology of mitral valve in older age groups (Rosenthal and Feigin), 346
- Patterns, electrocardiographic, diagnostic value of, based on assay of 261 additional autopsied cases (Katz et al.), 696
- Pectoris, angina, anatomic data regarding surgical treatment of, 876*
- peptic ulcer, and essential hypertension, relation of neurocirculatory dystonia to, 875*
- Pellagra-beriberi syndrome (3); cardiovascular manifestations of vitamin B deficiency in children in Cuba, 126*
- Penicillin, experiences in treatment of subacute bacterial endocarditis with (Greiger), 736
- in treatment of subacute bacterial endocarditis; further studies in twenty-one patients (Jimenes Romo), 736
- therapy, effects of anticoagulants on, pathologic lesion of subacute bacterial endocarditis, 550*
- treatment of acute bacterial endocarditis with, 880*
- of cardiovascular syphilis with, 555*
- Pentose isolated from heart muscle, note on (Sodi Pallares et al.), 705
- Pepsin, hypertension in dog, and hypertension in cow, conclusions based upon experiments with, 889*
- Peptic ulcer, essential hypertension, and angina pectoris, relation of neurocirculatory dystonia to, 875*
- ulcers, electrocardiographic findings in patients with, 397*

- Perfusion, coronary, with radioactive erythrocytes and glass spheres, collateral circulation of normal human heart by (II); studies on coronary circulation (Prinzmetal et al.), 420
- Periarteritis nodosa, report of case and comparison with respect to: temporal arteritis, 555*
- Pericardium, multiple liver abscesses with rupture into (Zodikoff), 375
- Peripheral and cerebral emboli, study of, registered in National Institute of Cardiology of Mexico (Mendez Hernandez), 712
- vascular disease and causal states, use of tetraethylammonium in, 406*
- disorders, medical management of, 392*
- Phantom limb, painful, treated by high cervical chordotomy, 393*
- Phonocardiography, apex cardiogram and its utility in (Aixala), 703
- Phosphorus, enzymatic liberation of, and ventricular oxygen consumption, significance of, in mechanism of digitalis effect (Guerra), 705
- Physical effort, cardiac asystole in normal young man following (Eichna et al.), 254
- Physiologic condition of heart in natives of high altitudes (Rotta), 669
- Pilots, older, electrocardiograms of, 129*
- Placement, selective, of patients with heart disease in competitive employment (Kossmann et al.), 700
- Plasma protein, total, hemoglobin and, changes in, after injection of mercuraphylline, 387*
- Plethysmograph, a new sensitive portable (Burch), 48
- Plethysmographic measurement of blood flow through forepaw during experimental shock (Kondo et al.), 207
- Pneumonectomy, cardiac arrhythmias complicating total, 879*
- Pneumothorax, spontaneous, and mediastinal emphysema, electrocardiographic phenomena associated with, 884*
- Poisoning, methyl alcohol, electrocardiographic changes associated with (Weisberger and MacLaughlin), 27
- Poliomyelitis, anterior, acute, heart in (Geffer et al.), 228
- nonfatal, clinical observations in 456 patients with (Geffer et al.), 228
- Polycythemia, cyanosis and, observations on volume of pulmonary circulation and its importance in production of (Taussig and Blalock), 413
- Post-tachycardia syndrome (Cossio and Berconsky), 720
- Postural heart block, 542*
- Potential, intracavity, in man and in dog, comparative study of (Sodi Pallares et al.), 819
- Precordial electrocardiogram, influence of non-indifferent electrode upon, 391*
- leads CF₂ and IV F, Nehb's leads, and leads from extremities, comparison between, with special regard to diagnosis of infarction, 888*
- different, comparative study of (Meneses Hoyos and Gonzalez Tomayo), 698
- importance of, in electrocardiograms after exertion in angina pectoris; action of certain drugs (trinitrin, aminophylline, and papaverine) (Battro and Araya), 723
- in children, 130*
- multiple, review of eight cases of Wolff-Parkinson-White syndrome including four cases with initial left ventricular activation as demonstrated by (Reed et al.), 701
- unipolar, electrocardiographic studies in rheumatic heart disease with reference to interpretation of (First et al.), 1
- of normal children, significance of downward T wave in, 395*
- significance of abnormally small QRS deflections in one or more (Lapin), 747
- unipolar, in normal individuals of both sexes, and at different ages, electrocardiographic studies in Puerto Rico with (Suarez), 731
- Prefibrillation, auricular (Gonzalez Sabathie and Gaspary), 720
- Pregnancy and heart disease (Laubry and Routier), 739
- complete heart block in (report of two successful deliveries), 545*
- Pregnant patient with mitral stenosis, pulmonary edema in (Peters and Penner), 528
- Premature contractions, first cardiac sound in (Cossio), 707
- Pressor test, value of, in high blood pressure (Taquini), 735
- Pressure, blood, levels of, in both arms and legs in normal subjects and patients suffering from certain disease, 884*
- Primary systemic amyloidosis, 392*
- Prostigmine, electrocardiographic effects of, 549*
- Prothrombin time, effect of salicylate administration on, 887*
- in man, effect of aminophylline on, 549*
- Prothrombinopenic effect of massive salicylate therapy in acute rheumatic fever, 127*
- Psychoneurotic patients, electrocardiographic study of, 553*
- Psychosomatic disability, is orthodox therapy of rheumatic fever conducive to? (Adamson), 715
- Puerto Rico, electrocardiographic studies in, with unipolar precordial leads in normal individuals of both sexes and at different ages (Suarez), 731

- Pulmonary arterial tree, congenital dilatation of; relation to Ayerza's disease and primary pulmonary arteriosclerosis, 397*
- artery, experimental stenosis of (Vaccarezza et al.), 728
- origin of left coronary artery from (Kaunitz), 182
- circulation, observations on volume of, and its importance in production of cyanosis and polycythemia (Tausig and Blalock), 413
- edema, acute, morphine treatment of (Gonzalez Sabathie), 738
- in pregnant patient with mitral stenosis (Peters and Penner), 528
- emboli, venous thrombosis and, in urology, 265*
- embolism in medical patients: comparison of incidence, diagnosis, and effects of treatment of 273 cases at Massachusetts General Hospital in two five-year periods (Carloti et al.), 737
- stasis in presence of mitral disease, micro-modulation, manifestation of, 389*
- stenosis, aortic stenosis, patent ductus arteriosus, and coarctation of aorta, differential diagnosis of (Kerr), 725
- (venous) air embolism (Durant et al.), 269
- ventilation, effect of, on anoxemia, 395*
- Pyruvate exchange of heart, influence of vitamin B₁ deficiency on (Randles et al.), 341
- Q**
- Q_s and QS₂ deflections in electrocardiogram: criteria and significance (Ungerleider and Gubner), 807
- QRS deflections, abnormally small, in one or more precordial leads, significance of (Lapin), 747
- QS₂ and Q_s deflections in electrocardiogram: criteria and significance (Ungerleider and Gubner), 807
- Q-T intervals, long, electrocardiograms with large, upright T waves and (Byer et al.), 796
- Quindine and digitalis in treatment of auricular fibrillation (Weisman), 719
- effects of, on circulatory system, 542*
- R**
- Radioactive erythrocytes and glass spheres, collateral circulation of normal human heart by coronary perfusion with (II); studies on coronary circulation (Prinzmetal et al.), 420
- Radiologic and clinical examinations, comparative studies with three types of electrocardiographic leads (classic, unipolar extremity leads, and multiple precordial leads) in relation to (Ramos et al.), 699
- Raynaud's disease in men (Abramson and Shumacker), 500
- Red blood corpuscles, weight of, in heart failure determined with labelled erythrocytes during and after decompensation (Nylin and Hedlund), 770
- Reflex, hyperactive carotid sinus, attacks of unconsciousness resulting from (Smith), 711
- Refrigeration in surgery, 876*
- Renal hypertension, 132 (B. Rev.)
- Renin, concentration of, in renal venous blood in patients with chronic heart failure, 878*
- Residual arrhythmias, benign (Gonzalez Sabathie and Gaspary), 729
- Resuscitation of isolated human heart; direct electrocardiography of heart during restoration, 547*
- Retinal and choroidal arterioles in malignant hypertension: a clinical and pathologic study of fifteen cases, 885*
- angiography in essential arterial hypertension (study of 300 clinical cases) (Puig Solanes), 733
- Rheumatic carditis, acute, in children, duration of electrical systole (Q-T) in (Taran and Szilagyi), 14
- disease, significance of interstitial lymphocytosis in, and in other inflammatory processes (Costero), 717
- encephalopathy, 887*
- fever, acute, prothrombinopenic effect of massive salicylate therapy in, 127*
- heart disease in children in rural town country, particularly in relation to, 888*
- in Naval enlisted personnel; II. Effectiveness of intensive salicylate therapy in cases of acute infection, 388*
- incidence and clinical features of, in Mexico City (Robles Gil), 713
- is orthodox therapy of, conducive to psychosomatic disability? (Adamson), 715
- statistical analysis of incidence during sulfadiazine prophylaxis, 551*
- sudden death in, 396*
- heart disease, electrocardiographic studies in, with reference to interpretation of multiple unipolar precordial leads (First et al.), 1
- patient, encephalopathy of (de Gortari et al.), 716
- valvular endocarditis, clinical features of 1,160 cases of (Cortes and Villarreal), 715
- Rhythm, atrionodal, with ventricular bigeminy (Perelman and Miller), 34
- Rhythmic alteration in direction of ventricular complexes, on mechanism of paroxysmal tachycardia with (Zimdahl and Kramer), 218
- Roentgen diagnosis of aneurysm of abdominal aorta, significance of calcification for, 887*
- of double aortic arch and other anomalies of great vessels, 129*

- Roentgenologic kymographic studies of heart in presence of arteriovenous fistula and their interpretation, 550*
- Roentgenology, clinical, of heart, 410 (B. Rev.)
- RS-T interval, reversible changes in, during severe acidosis caused by administration of carbon dioxide; tolerance of human heart to acidosis (Altschule and Sulzbach), 458
- Rupture into pericardium, multiple liver abscesses with (Zodikoff), 375
- traumatic, of aorta (Strassmann), 508

S

- Salicylate administration, effect of, on prothrombin time, 887*
- sodium, influence of, on antigen-antibody reaction, 889*
- therapy, intensive, effectiveness of, in cases of acute infection (II); rheumatic fever in Naval enlisted personnel, 388*
- massive, in acute rheumatic fever, prothrombinopenic effect of, 127*
- Sarcoid, Boeck's, electrocardiographic and spirometric findings, 877*
- Scalenotomy, an analysis of eleven cases done for scalenus anticus syndrome, 876*
- Scalenus anticus syndrome, scalenotomy, 876*
- Scleroderma, diffuse, with involvement of heart (Mathisen and Palmer), 366
- Septal defects, interauricular, in dogs, experimental method for closure of (Cohn), 453
- Septum, interventricular, perfection of, in case of subacute bacterial endocarditis (Levy, II, and Hull), 856
- Serum cholesterol concentration, cholesterol content of human aorta in relation to, 888*
- Shock accompanying myocardial infarction, treatment of (Schwartz), 169
- and hemorrhage, effect of, on caliber of abdominal vena cava, 878*
- experimental, plethysmographic measurement of blood flow through forepaw during (Kondo et al.), 207
- myocardial depression in (Wiggers), 633
- Sinoauricular block (Gonzalez Sabathie and Gaspari), 732
- Sinus reflex, hyperactive carotid, attacks of unconsciousness resulting from (Smith), 711
- Size, heart, influence of, on circulation time (Nathanson and Elek), 464
- of heart and velocity of blood, relation between (Meneely and Chesnut), 175
- Smoking, effect of, on vasodilatation produced by oral administration of 95 per cent ethyl alcohol or a substantial meal (Roth and Sheard), 654
- Snake venom, Central American, cardiac action of (Garcia Carrillo), 709
- Sodium salicylate, influence of, on antigen-antibody reaction, 889*
- Soldiers, young, sudden and unexpected deaths of, 882*
- Sotradecol, sodium alkyl sulfate solution, clinical evaluation of, in injection therapy of varicose veins, 544*
- Sound tracings and simultaneous electrocardiograph of mother, congenital complete heart block diagnosed in utero with (Jordan and Randolph), 109
- Spheres, glass, collateral circulation of normal human heart by coronary perfusion with radioactive erythrocytes and (II); studies on coronary circulation (Prinzmetal et al.), 420
- Spinal anesthesia, evaluation of certain drugs used to maintain blood pressure during, 264*
- cord, vascular tumours of, associated with skin hemangiomata, 393*
- Spirometric and electrocardiographic findings in Boeck's sarcoid, 877*
- Starvation, myocardial damage in, 877*
- Stenosis, experimental, of pulmonary artery (Vaccarezza et al.), 728
- mitral, pulmonary edema in pregnant patient with (Peters and Penner), 528
- studies on heart sound in (Meneses Hoyos et al.), 706
- with auricular fibrillation, cardiac asthma and acute edema of lungs in (Berconsky and Neuman), 738
- pulmonic, congenital, surgical treatment of, 551*
- Sternal depression, heart in, 403*
- Steroids, influence of, on restoration of hypertension in hypophysectomized rats, 881*
- Stimulation, ventricular, and contraction, sequence of, in case of anomalous atrioventricular excitation (Kossman and Goldberg), 308
- Strain, acute right ventricular, spontaneous mediastinal emphysema with (Klein), 867
- Streptomycin in treatment of subacute bacterial endocarditis, 404,* 541*
- Subacute bacterial endocarditis, experiences in treatment of, with penicillin (Greiger), 736
- penicillin in treatment of; further studies in twenty-one patients (Jimenes Romo), 736
- perforation of interventricular septum in case of (Levy, II, and Hull), 856
- Subclavian artery, role of clavicle in occlusion of, 124*
- Sulfadiazine administration, effect of, on cardiac function in dog (Hafkesbring and Wertenberger), 93
- prophylaxis, statistical analysis of incidence during: rheumatic fever, 551*
- Sulfamerazine administration, effect of, on cardiac function in dog (Hafkesbring and Wertenberger), 93
- Sulfapyridine administration, effect of, on cardiac function in dog (Hafkesbring and Wertenberger), 93

Sulfapyrazine administration, effect of, on cardiac function in dog (Hafkes-bring and Wertenberger), 94

Sulfathiazole administration, effect of, on cardiac function in dog (Hafkes-bring and Wertenberger), 93

Sulfonamide administration, effect of, on cardiac function in dog (Hafkes-bring and Wertenberger), 84

Sulfonamides, myocardial changes following, 392*

Sulfuric ether, memoir on new use of, 133 (B. Rev.)

Surgery of autonomic nervous system, indications and results of, in Naval personnel, 265*

refrigeration in, 876*

results of, in patent ductus arteriosus (Shapiro and Johnson), 725

Surgical anesthesia, centennial of, annotated catalogue, 133 (B. Rev.)

approach to hypertension, 266*

aspects of trench foot, 394*

significance of aortic arch anomalies, 404*

treatment of ascites, 401*

of congenital pulmonic stenosis, 551*

of gangrene in trench foot, 406*

role of, in management of hypertension (Peet and Isberg), 735

Symbols, writing, to describe cardiovascular sounds and murmurs while listening (Segall), 705

Sympathectomy in hypertension, anesthesia for, 398*

Sympathomimetic amines in heart muscle: pathogenic and therapeutic significance (Raab), 707

Synchronization of auricular and ventricular beats during complete heart block (Segers et al.), 685

Syndrome, anginal, further observations on treatment of, with thiouracil (Ben-Asher), 490

Lutembacher's, complicated by acute bacterial endocarditis (Geiger and Anderson), 240

post-tachycardia (Cossio and Berconsky), 720

scalenus anticus, scalenotomy, 876*

Wolff-Parkinson-White, presenting certain unusual features (Cain), 523

review of eight cases of, including four cases with initial left ventricular activation as demonstrated by multiple precordial leads (Reed et al.), 701

Syphilis, untreated in male Negro; evidence of cardiovascular abnormalities and other forms of morbidity, 882*

Systemic circulation in man, observations on dynamics of, 881*

Systole, electrical (Q-T), duration of, in acute rheumatic carditis in children (Taran and Szilagyi), 14

T

T waves, abnormal, study of, in patients presenting no evidence of organic heart disease, 546*

downward, in precordial leads of normal children, significance of, 395*

electrocardiograms with large, upright, and long Q-T intervals. (Byer et al.), 796

inverted, effect of nitrites and exercise on, 402*

Tachycardia, intermittent ventricular, in youth; report of case with fatal termination (Maddox), 739

paroxysmal auricular, congestive heart failure and death in case of (Grant), 121

congenital (Garvin and Kline), 362

transitory flutter and fibrillation, 884*

ventricular, intravenous use of morphine in treatment of (Gonzalez Sabathie), 719

with rhythmic alternation in direction of ventricular complexes, on mechanism of (Zimdahl and Kramer), 218

with syncope, 391*

produced by venous hypertension in man: study of Bainbridge reflex, 548*

Test, pressor, value of, in high blood pressure (Taquini), 735

Tetraethylammonium, use of, in peripheral vascular disease and causalgic states, 406*

Tetrahedron, substitution of, for Einthoven triangle (Wilson et al.), 594

Tetralogy of Fallot (Middleton and Ritchie), 250

Thiouracil, further observations on treatment of anginal syndrome with (Ben-Asher), 490

Thiourea derivatives, two, influence of, on blood pressure in hypertensive rats, 128*

Thoracic blood vessels and heart, foreign bodies in and in relation to, 124*

Thromboangiitis obliterans, clinical impression of therapy in (McGovern), 712

diagnosis and treatment of, in vascular centers of Army General Hospitals (Freeman), 332

in Negro (Breidenbach, Jr., and Palmer), 849

thrombophlebitis of deep veins in, 406*

Thrombo-embolic lesions accompanying myocardial infarction, incidence of (Hellerstein and Martin), 443

Thrombophlebitis, femoral, late results of, and their treatment, 395*

of deep veins in thromboangiitis obliterans, 406*

Thrombosis, acute coronary, treatment of, with dicumarol (Nichol), 722

Time, circulation, influence of heart size on (Nathanson and Elek), 464

- Tolerance of human heart to acidosis; reversible changes in RS-T interval during severe acidosis caused by administration of carbon dioxide (Altschule and Sulzbach), 458
- Tracer substances, fluorescent, objective clinical procedure for determination of circulation velocity using (Winsor et al.), 704
- Transmural involvement, complete and incomplete, electrocardiographic features of myocardial infarction as affected by involvement of septum and by, 401*
- Traumatic rupture of aorta (Strassmann), 508
- Treatment, morphine, of acute pulmonary edema (Gonzalez Sabathie), 738
- of acute bacterial endocarditis with penicillin, 880*
- of anginal syndrome with thiouracil, further observations on (Ben-Asher), 490
- of shock accompanying myocardial infarction (Schwartz), 169
- surgical, role of, in management of hypertension (Peet and Isberg), 735
- Trench foot, surgical aspects of, 394*
- treatment of gangrene in, 406*
- Triangle, Einthoven, substitution of tetrahedron for (Wilson et al.), 594
- Tricuspid disease, cardiac failure in (Taquini), 727
- insufficiency, new diagnostic sign of (Rivero Carvallo), 728
- sign of, 881*
- of Ebstein type report of case of, with probable fetal endocarditis and exceptional electrocardiographic characteristics (Berber), 726
- valvular lesions, clinical diagnosis of, 543*
- Trinitrin, aminophylline, and papaverine, action of certain drugs; importance of precordial leads in electrocardiograms after exertion in angina pectoris (Battro and Araya), 723
- Tuberculosis, pulmonary, significance of concordant inverted ventricular deflections in electrocardiogram of patients with, 402*
- U
- Ulcer of leg due to arteriosclerosis and ischemia, occurring in presence of hypertensive disease (hypertensive-ischemia ulcers), 266*
- peptic, essential hypertension, and angina pectoris, relation of neurocirculatory dystonia to, 875*
- Unconsciousness, attacks of, resulting from hyperactive carotid sinus reflex (Smith), 711
- Unipolar precordial leads in normal individuals of both sexes and at different ages, electrocardiographic studies in Puerto Rico with (Suarez), 731
- multiple, electrocardiographic studies in rheumatic heart disease with reference to interpretation of (First et al.), 1
- Uremia, heart in (Langendorf and Pirani), 282
- Urinary extracts of normal and hypertensive individuals and of hypertensive dogs, action of, upon arterial pressure, 391*
- Urology, venous thrombosis and pulmonary emboli in, 265*
- V
- Valvular endocarditis, rheumatic, clinical features of 1,160 cases of (Cortes and Villarreal), 715
- lesions, tricuspid, clinical diagnosis of, 543*
- Varicose veins, clinical evaluation of Sotradecol, sodium alkyl sulfate solution, in injection therapy of, 544*
- Vascular centers of Army General Hospitals, diagnosis and treatment of thromboangiitis obliterans in (Freeman), 332
- tumors of spinal cord associated with skin hemangiomata, 393*
- Vasodilation, effect of smoking on, produced by oral administration of 95 per cent ethyl alcohol or a substantial meal (Roth and Sheard), 654
- Vein, artery, and bone marrow, blood cultures made from, comparative study of, in patients with subacute bacterial endocarditis (Salazar Mallén et al.), 692
- Velocity, circulation, objective clinical procedure for determination of, using fluorescent tracer substances (Winsor et al.), 704
- of blood, relation between size of heart and (Meneely and Chesnut), 175
- Vena cava, abdominal, effect of hemorrhage and shock on caliber of, 878*
- Venesection, effects of, in low output heart failure, 878*
- Venom, snake, cardiac action of Central American (Garcia Carillo), 709
- Venous hypertension in man, tachycardia produced by; study of Bainbridge reflex, 548*
- pulmonary, air embolism (Durant et al.), 269
- thrombosis, 545*
- after infusion with gelatin solutions containing mercurial preservatives, 542*
- and pulmonary emboli in urology, 265*
- Ventricle, various components of monophasic electrocardiogram of, 885*
- Ventricular activation, initial left, as demonstrated by multiple precordial leads, review of eight cases of Wolff-Parkinson-White syndrome including four cases with (Reed et al.), 701
- and auricular beats, synchronization of, during complete heart block (Segers et al.), 685
- bigeminy, atrionodal rhythm with (Perelman and Miller), 34
- complexes, on mechanism of paroxysmal tachycardia with rhythmic alternation in direction of (Zimdahl and Kramer), 218

Ventricular—Cont'd

- contraction, observations on (Kossmann and Goldberg), 313
 - excitation, observations on (Kossmann and Goldberg), 308
 - gradient and medium axis, easy method for calculating value of (Meneses Hoyos), 699
 - hypertrophy, intrinsic deflection in normal cases and in, 886*
 - oxygen consumption and enzymatic liberation of phosphorus, significance of, in mechanism of digitalis effect (Guerra), 705
 - right auricular and, pressure in man, first recording of curves of, 127*
 - stimulation and contraction, sequence of, in case of anomalous atrioventricular excitation (Kossmann and Goldberg), 308
 - strain, acute right, spontaneous mediastinal emphysema with (Klein), 867
 - tachycardia, intermittent, in youth; report of case with fatal termination (Maddox), 739
 - paroxysmal, intravenous use of morphine in treatment of (Gonzalez Sabathie), 719
- Vertebral vessels, arteriovenous aneurysm of, 543*
- Victory over pain, 132 (B. Rev.)
- Vitamin B deficiency, cardiovascular manifestations of, in children of Cuba;
1. So-called borderline case, 125*
 2. Acute beriberi of nursing, 125*
 3. Pellagra-beriberi syndrome, 126*
 4. So-called idiopathic cardiac hypertrophy, 126*

- B₁, amount of, in urine of cardiovascular patients who do not present a frank syndrome of avitaminosis or of hypovitaminosis but are nevertheless clinically improved by administration of this vitamin (B₁), 544*
- deficiency, influence of, on pyruvate exchange of heart (Randles et al.), 341
- E deficiency, electrocardiogram of rats on, 881*

- Volume elasticity of aorta in intact dog (Katz et al.), 319
- of pulmonary circulation and its importance in production of cyanosis and polycythemia, observations on (Taussig and Blalock), 413

W

- War wounds of arteries, 265*
- Wolff-Parkinson-White syndrome presenting certain unusual features (Cain), 523
- review of eight cases of, including four cases with initial left ventricular activation as demonstrated by multiple precordial leads (Reed et al.), 701

Y

- Young man, normal, cardiac asystole in, following physical effort (Eichna et al.), 254

JUN 6 1947

MEDICAL LIBRARY

INDEX NUMBER

VOL. 33

JUNE, 1947

No. 6

AMERICAN HEART JOURNAL

For the Study of the
CIRCULATION



THOMAS M. McMILLAN . . Editor-in-Chief

Associate Editors

WALLACE M. YATER

SAMUEL BELLET

LOUIS B. LAPLACE

EDITORIAL BOARD

EDGAR V. ALLEN

ALFRED BLALOCK

CLARENCE E. DE LA CHAPELLE

HARRY GOLDBLATT

TINSLEY R. HARRISON

T. DUCKETT JONES

LOUIS N. KATZ

EUGENE M. LANDIS

JOHN K. LEWIS

H. M. MARVIN

JONATHAN C. MEAKINS

ROY W. SCOTT

ISAAC STARR

PAUL D. WHITE

FRANK N. WILSON

CHARLES C. WOLFERTH

IRVING S. WRIGHT

Published Monthly Under the Editorial Direction of The American Heart Association

Copyright 1947 by The C. V. Mosby Company, Jefferson City, Mo., and St. Louis, U. S. A.

Contents on Inside Cover

American Heart Journal

CONTENTS FOR JUNE, 1947

Original Communications

- Significance of Abnormally Small QRS Deflections in One or More Precordial Leads. Albert W. Lapin, M.D., Montreal, Quebec..... 747
- Weight of the Red Blood Corpuscles in Heart Failure Determined With Labelled Erythrocytes During and After Decompensation. G. Nylin, M.D., and S. Hedlund, M.D., Stockholm, Sweden..... 770
- Electrocardiograms With Large, Upright T Waves and Long Q-T Intervals. Edwin Byer, M.D., Richard Ashman, Ph.D., and Louis A. Toth, Ph.D., New Orleans, La..... 796
- The Q₃ and QS₂ Deflections in the Electrocardiogram: Criteria and Significance. Harry E. Ungerleider, M.D., and Richard Gubner, M.D., New York, N. Y.. 807
- Comparative Study of the Intracavity Potential in Man and in Dog. Demetrio Sodi Pallares, M.D., Mario Vizecaino, M.D., Jorge Soberon, M.D., and Enrique Cabrera, M.D., Mexico, D.F., Mexico..... 819

Clinical Reports

- Thromboangiitis Obliterans in the Negro: Report of a Case and Review of the Literature. Warren C. Breidenbach, Jr., M.D., and Dwight M. Palmer, M.D., Columbus, Ohio..... 849
- Perforation of the Interventricular Septum in a Case of Subacute Bacterial Endocarditis. Louis Levy, II, M.D., and Edgar Hull, M.D., New Orleans, La..... 856
- Dissecting Aneurysm With Hemopericardium. George M. Ellis, M.D., Toledo, Ohio..... 860
- Spontaneous Mediastinal Emphysema With Acute Right Ventricular Strain. Arthur Klein, M.D., Richmond, Va..... 867

Abstracts and Reviews

- Selected Abstracts..... 875
- American Heart Association, Inc..... 890

Index

- Index..... 891

American Heart Journal

For the Study of the Circulation

THOMAS M. McMILLAN, M.D., Editor-in-Chief

Clinton Street Bldg., Pennsylvania Hospital, 330 S. 9th Street, Philadelphia 7, Pa.

Associate Editor

WALLACE M. YATER, M.D.
1150 Connecticut Avenue, N. W.
Washington 6, D. C.

Associate Editor

SAMUEL BELLET, M.D.
2021 Spruce Street
Philadelphia 3, Pa.

Associate Editor

LOUIS B. LAPLACE, M.D.
200 Glenn Road
Ardmore, Pa.

EDITORIAL COMMUNICATIONS

Original Communications.—Manuscripts for publication, letters, and all other communications relating to the editorial management of the Journal should be sent to the Editor in-Chief, Dr. Thomas M. McMillan, Clinton Street Bldg., Pennsylvania Hospital, 330 S. 9th Street, Philadelphia 7, Pa. Articles are accepted for publication with the understanding that they are contributed solely to the American Heart Journal.

Neither the editor nor the publisher accepts responsibility for the views and statements of authors whose manuscripts are published as "Original Communications."

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double spacing and liberal margins. References should be placed at the end of the article and should consist of the name of the author, the title of the article, and the name, volume number, page number, and year of publication of the journal, in that order. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked on the margin or back with the author's name.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the editor for color plates, elaborate tables, or extra illustrations. To insure clear reproduction, all copy for zinc cuts, including pen drawings and charts, must be prepared with India ink, and a black ribbon must be used for typewritten material. Only good photographic prints or original drawings should be supplied for half-tone work.

Exchanges.—Contributions, letters, exchanges, reprints, and all other communications relating to the Abstract Department of the Journal should be sent to Dr. Thomas M. McMillan, Clinton Street Bldg., Pennsylvania Hospital, 330 S. 9th Street, Philadelphia 7, Pa. Writers on subjects which are related in any way to cardiovascular disease are requested to place this address on their permanent reprint mailing lists.

Reprints.—Reprints of articles published among "Original Communications" must be ordered specifically, in separate communication to The C. V. Mosby Co., 201 Madison St., Jefferson City, Mo., and 3207 Washington Blvd., St. Louis 3, U. S. A., who will send their schedule of prices. Individual reprints of an article must be obtained through the author.

Review of Books.—Publishers and authors are informed that the space of the Journal is so fully occupied by matter pertaining to the branches to which it is devoted that only works treating of these subjects can be noticed. Deserving books and monographs on physiology, pathology, and diseases of the heart, circulation, blood, and blood vessels will be reviewed when space is available. Send books to the Editor-in-Chief, Dr. Thomas M. McMillan, Clinton Street Bldg., Pennsylvania Hospital, 330 S. 9th Street, Philadelphia 7, Pa.

BUSINESS COMMUNICATIONS

Business Communications.—All communications in regard to advertising, subscriptions, change of address, etc., should be addressed to the Publishers.

Subscription Rates.—Single copies, 85 cents; in the United States and countries in U. S. Postal Zone, \$10.00 per annum in advance; Canada and Other Foreign Countries, \$11.00.

Remittances.—Remittances for subscriptions should be made by check, draft, post office or express money order, payable to the publishers.

Change of Address.—The publishers should be advised of change of subscriber's address about fifteen days before the date of issue, with both new and old addresses given.

Advertisements.—Only articles of known scientific value will be given space. Forms close tenth of month preceding date of issue. Advertising rates and page sizes on application.



STERILIZE the stopper, insert a sterile hypodermic needle, and withdraw the required dose. It is that simple to prepare an injection of B complex vitamins from Ampoules 'Betalin Complex' (Vitamin B Complex, Lilly). This prepared solution contains the five most essential vitamins of the B complex in convenient, ready-to-use, 10-cc. rubber-stoppered ampoules.

Each cc. contains:

Thiamin Chloride	5 mg.
Riboflavin	2 mg.
Nicotinamide	75 mg.
Pantothenic Acid (as Calcium Pantothenate)	2.5 mg.
Pyridoxine Hydrochloride (Vitamin B ₆ Hydrochloride)	5 mg.

The date appearing on each package of Ampoules 'Betalin Complex' indicates the period for which the solution will retain full potency provided it is properly stored.

Ampoules 'Betalin Complex' may be used intravenously or intramuscularly and, when added to dextrose infusions, will prevent acute avitaminosis. They are quickly available through your usual source of medical supplies.

Lilly

ELI LILLY AND COMPANY, INDIANAPOLIS 6, INDIANA, U.S.A.

